Synthesis and Spectral Studies of Methyl Heterocyclic Systems

by

Paul P. Doyle, B.Sc. (Brock University)

A thesis
submitted to the Department of Chemistry
in partial fulfilment of the requirements
for the degree of
Master of Science

May 1979

Brock University
St. Catharines, Ontario

dedicated to

Pat, Ann, Liz and Fran

Thanks to Ian D. Brindle for his support and encouragement throughout the project.

Special thanks to Tim Jones for obtaining mass and NMR spectra.

And a very special thanks go to my parents, Pat and Ann, and to Elizabeth and Frances for their encouragement, patience and understanding.

Port Colborne, Ontario.

May 1979.

Table of Contents

List of Tables

List of Figures

Abstract

2-Carboxy-2'-methyldiphenyl sulfide was prepared by the Ullmann reaction and cyclodehydrated by sulfuric acid to afford 4-methylthioxanthone. 1-Methylthioxanthone was separated from the reaction mixture obtained upon cyclodehydration of 2-carboxy-3'-methyldiphenyl sulfide. In addition, 1-, 2-, 3- and 4-methylthioxanthone 10,10-dioxides were synthesized by oxidation of the corresponding thioxanthones.

o-, m- and p-N-Tolylanthranilic acids were prepared by the Ullmann reaction and used as precursors for the preparation of 1-, 2- and 4-methyl-9-chloroacridine and finally 1-, 2-, 3- and 4-methylacridone.

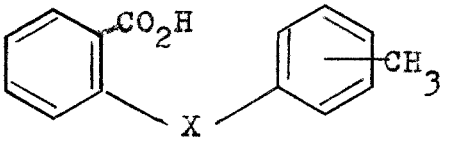
High resolution, 60 MHz PMR spectra were obtained on the four monomethyl isomers of xanthone, thioxanthone, thioxanthone 10,10-dioxide and acridone, and on 1-, 2- and 4-methyl-9-chloroacridine. For some compounds, coupling of all three different aromatic protons to the methyl was observed, two of the couplings typically being smaller than the third. With the large (ortho) coupling being on the order of 0.5 to 1.0 Hz, it was necessary to decouple the aromatic part of the spectrum. The magnitude of the ortho benzylic constant may be related to an incomplete π-bond delocalization in the molecules.

INTRODUCTION

Long Range Coupling

Spin-spin coupling in ^1H NMR spectroscopy has been recognized for some time as a useful technique for structural determination. Nevertheless, the coupling between an aromatic methyl and a ring proton has not been widely studied.

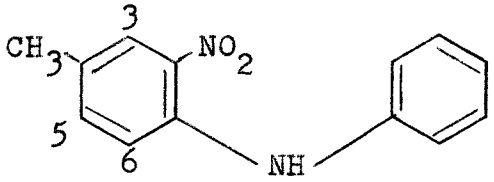
^1H NMR spectra of methyl-substituted benzenes, phenols, thiophenols and anilines have been studied, however, long-range proton-proton couplings between the aromatic methyl and ring protons have not been widely documented. Similarly, such couplings have not been observed in monomethyl analogues of salicylic, thiosalicylic and anthranilic acids. From the foregoing observations, it is not difficult to understand why this type of coupling has not been reported for the various isomers of the compounds of type I.



(I)

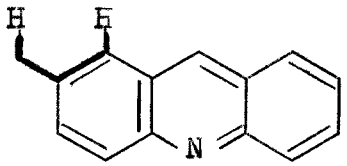
(X = O, S, or NH)

Recently, this type of coupling has been observed by several groups. Spragg[1] observed the methyl signal of II at 90 MHz in $CDCl_3$ to appear surprisingly as a doublet despite the presence of two ortho protons. In the aromatic region the signal H-3 only could be identified, and decoupling of this proton collapsed the CH_3 resonance to a singlet with 0.5 Hz linewidth.

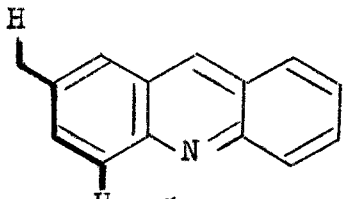


(II)

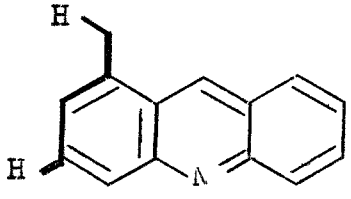
Only a few ^{1}H NMR long-range coupling studies of methyl heterocyclic systems have been reported. Sciacovelli and von Philipsborn have reported PMR data for the five monomethylacridine derivatives.[3] These authors have measured the absolute values for the ortho-, meta- and para-H, CH_3 long-range coupling constants at 100 MHz in $CDCl_3$. They use the following nomenclature to describe the geometry of the pathway responsible for this particular spin-spin coupling.*



$^{4}J_{cc}$

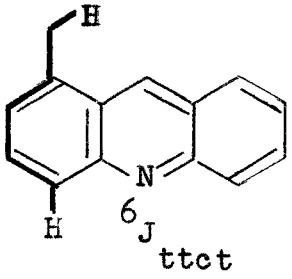


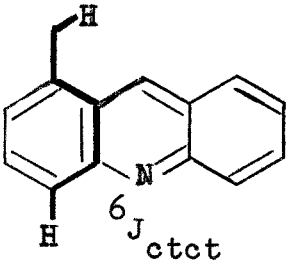
$^{5}J_{ttt}$



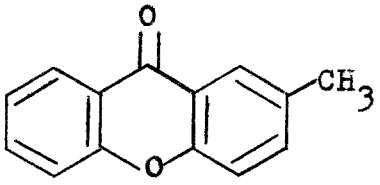
$^{5}J_{ctt}$

* c and t stand for cis and trans arrangement respectively of a three bond fragment.





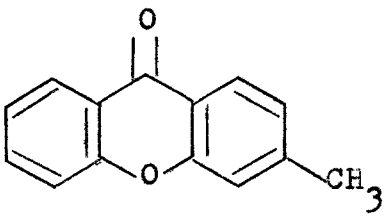
Initial work which prompted the present investigation was presented by Vines.[4] While routine PMR spectra were being obtained, it was observed that the methyl group of 2-methylxanthone (III) at 60 MHz appeared as a



(III)

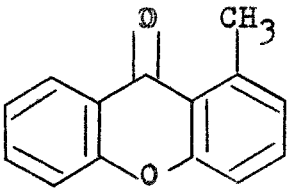
doublet (J ≃ 0.5 Hz). Irradiation of the CH_3 produced decoupling in the low field protion of the aromatic region (490 Hz). Irradiation of this low field proton collapsed the doublet.

The methyl group in 3-methylxanthone (IV) appeared to be rather broad. Double irradiation showed that splitting did occur and that it was caused by protons that absorbed in the high field portion of the aromatic region (423 Hz).



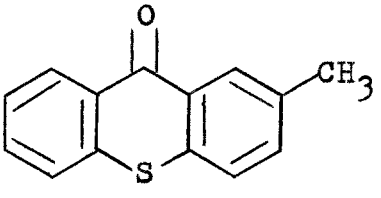
(IV)

The 1-methylxanthone (V) methyl appeared as a triplet with coupling ≃ 0.4 Hz. Spin decoupling of the methyl group gave decoupling in the high field portion of the aromatic region of the spectrum (420 Hz).



(V)

Finally, 2-methylthioxanthone (VI) showed a doublet for the methyl group with a coupling of 0.8-0.9 Hz. Irradiation of the CH_3 produced decoupling in the low field portion of the aromatic region (503 Hz).

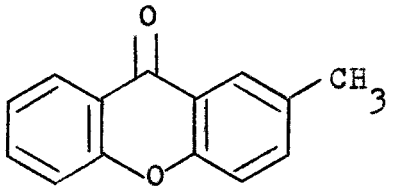


(VI)

Vines, however made no attempt to assign the protons doing the coupling.

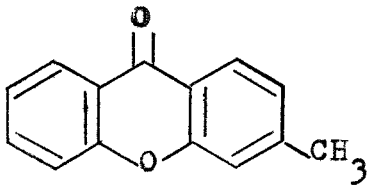
A follow-up study was undertaken by Brindle, Jones and Miller[5] in an attempt to elucidate the assignment of the protons doing the long range couplings that Vines had reported. They observed for some of the compounds, coupling of all three different aromatic protons to the methyl protons, two of the couplings typically being smaller than the third. However, with even the larger coupling being on the order of 0.5-0.8 Hz, it was necessary to decouple two distinctly different regions of the aromatic part of the spectrum.

The methyl group of 2-methylxanthone in the 60 MHz spectrum appeared surprisingly as a rather broad peak with shoulders. Irradiation of the methyl group gave decoupling in the low field and high field portions of the aromatic region of the spectrum. Subsequent irradiation of the high



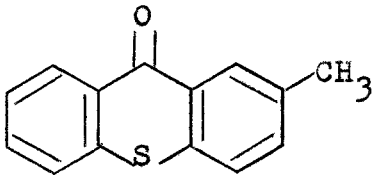
field portion (H-3) produced a doublet (J = 0.55 Hz) in the methyl region.

Coupling of both ortho protons in 3-methylxanthone again complicated the methyl absorption. Decoupling of protons H-2 and H-1 separately gave an unresolved peak but when a double irradiation of protons H-1 and H-2 was performed, a doublet was observed in the methyl region (J = 0.55 Hz).

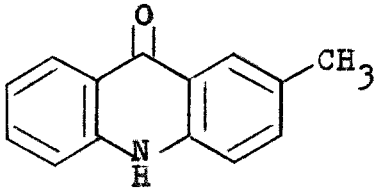


The group was unable to resolve the 1-methylxanthone methyl by any single or double irradiation. This methyl appeared as a multiplet with coupling ≃ 0.2 Hz.

2-Methylthioxanthone (VI) and 2-methylacridone (VII) showed a doublet for the methyl group with couplings of 0.77 and 0.82 Hz respectively. Irradiation of the CH_3 produced some decoupling in the low field portion

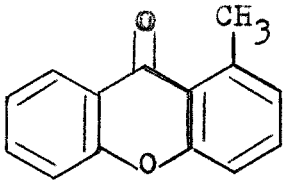


(VI)



(VII)

of the aromatic region, which they ascribed to the proton adjacent to the carbonyl, H-1. Irradiation of this proton subsequently collapsed the doublet. Supportive evidence for the assignment of H-1 was the absence of the low field multiplet in the spectrum of 1-methylxanthone (V).



(V)

Synthesis

All the monomethylxanthones have been reported in the literature. The standard synthetic route involves the cyclodehydration of a 2-carboxy-x'-methyldiphenyl ether, obtained from the condensation of o-chlorobenzoic acid and an appropriate cresol under Ullmann Reaction conditions.

Only the 2-methyl isomer of thioxanthone has been reported to date. To obtain the other monomethyl analogs, using a similar route, the unreported 2'- and 3'-methyl isomers of 2-carboxy-diphenyl sulfide had to first be prepared from the condensation of o-chlorobenzoic acid with the required thiocresol, then cyclodehydrated.

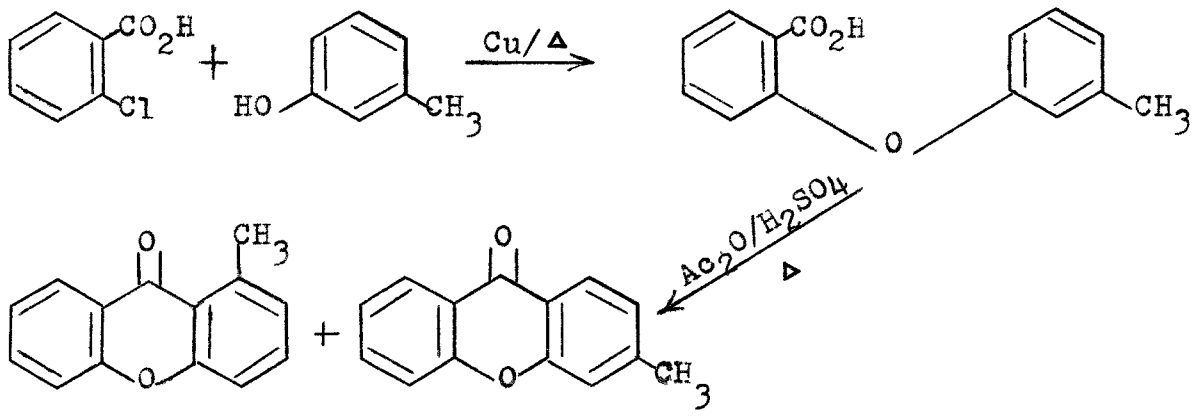
Unambiguous literature syntheses of 2- and 4-methylthioxanthone 10,10-dioxides are available, however the 1- and 3-methyl isomers had yet to be prepared and characterized.

All monomethylacridones have been reported synthesized. A widely used route to the acridones begins with an N-tolylanthranilic acid prepared from o-chlorobenozic acid and a toluidine. The conversion of the N-tolylanthranilic acid to a methyl-9-chloroacridine, followed by aqueous acid hydrolysis affords the desired acridone.

DISCUSSION

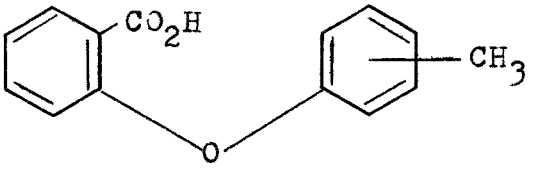
2.1 Synthesis

The most widely used method of preparing xanthones is the condensation of o-chlorobenzoic acid with phenols. The "dry" method in which the o-chlorobenzoic acid, phenol, and copper catalyst were added in this order to hot methanol containing three moles of sodium methoxide, was originally employed by Ullmann and his collaborators.[6] The methanol was distilled off, the glutinous residue heated for a short time at 180-200°, and the product isolated in the usual fashion. Various cyclising agents can be used on the resultant 2-carboxy-diphenyl ethers; however the most common are sulfuric acid or acetic anhydride containing sulfuric acid.[7,8] The 2-carboxy-x'-methyldiphenyl ethers were prepared by the Ullmann reaction as outlined by Goldberg and Wragg, using nitrobenzene as diluent.[7] Typically, the condensation of o-chlorobenzoic acid with m-cresol under Ullmann conditions gave 2-carboxy-3'-methyldiphenyl ether. Cyclisation of a 3'-substituted 2-carboxydiphenyl ether may give a 1- or 3-substituted xanthone according to whether ring closure takes place on the 2'- or 6'-position. 2-Carboxy-3'-methyldiphenyl ether cyclised in refluxing acetic anhydride to give a mixture of two methylxanthones. These were separated by column chromatography into the less polar 1-methylxanthone, and the more polar 3-methylxanthone, with a slight predominance of the 1-isomer.



Work-up after cyclisation with acetic anhydride proved to be very laborious and provided only a modest yield (20% or less) of the xanthone. Repetition of the cyclodehydration of 2-carboxy-4'-methyldiphenyl ether was performed using sulfuric acid.[6] The results showed that ring closure gives an 82% yield of 2-methylxanthone after one hour at 100°.

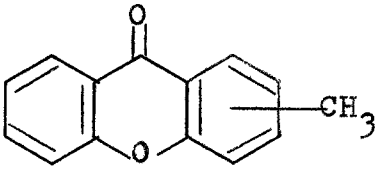
Table 1
2-Carboxy-x'-methyldiphenyl Ethers[a]



Isomer	Yield (%)	M.P.	Lit. M.P. (Ref.)
2'-methyl	58	130-132°	133.5° (6)
3'-methyl	56	96-97°	95° (7)
4'-methyl	75	126-128°	118.5° (6)

[a] All compounds were previously prepared during B.Sc. research and experimental details can be obtained in reference 9.

Table 2
Methylxanthones[a]

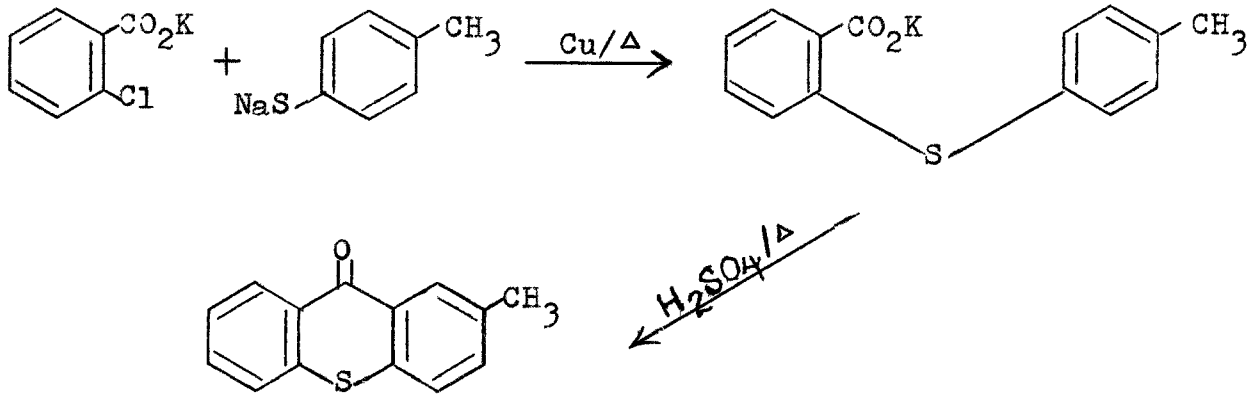


Isomer	Yield (%)	M.P.	Lit. M.P. (Ref.)
1-methyl	7[b]	113-114°	114° (7)
2-methyl	20	123-124°	121° (6)
3-methyl	3[b]	96-98°	97° (7)
4-methyl	10	125°	126° (6)

[a] All compounds were previously prepared during B.Sc. research and experimental details can be obtained in reference 9.

[b] Individual yield from the separated mixture.

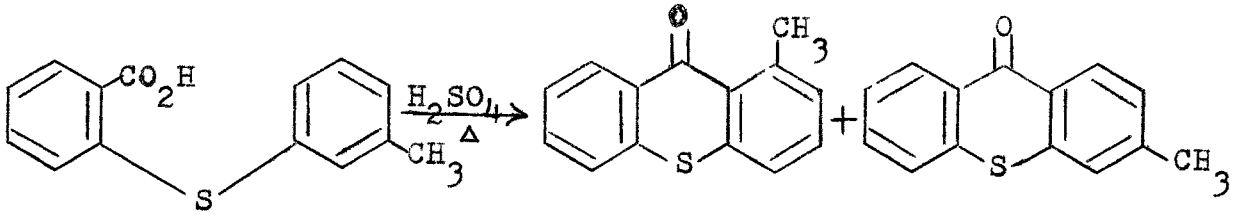
Goldberg first used the method of Ullmann to prepare a 2-carboxydiphenyl sulfide.[10] The condensation of the potassium salt of o-chlorobenzoic acid and the sodium salt of p-thiocresol was effected at elevated temperatures in the presence of a trace of copper powder. Mayer prepared a 2-carboxydiphenyl sulfide by a similar procedure and cyclised



this intermediate with sulfuric acid to produce the required thioxanthone.[11]

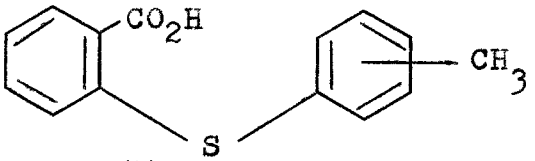
Typically, 2-carboxy-3'-methyldiphenyl sulfide was prepared by the reaction of the potassium salt of o-chlorobenzoic acid and the sodium salt of m-thiocresol under Ullmann conditions, using nitrobenzene as diluent.

When 2-carboxy-3'-methyldiphenyl sulfide was cyclised with sulfuric acid, a mixture of 1- and 3-methylthioxanthones in a ratio of ≃ 55:45 (as



determined by PMR spectra) was obtained. Column chromatography readily separated this yellow material into the less polar 1-methylthioxanthone and the more polar 3-methylthioxanthone.

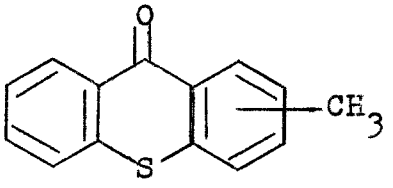
Table 3.
2-Carboxy-x'-methyldiphenyl Sulfides



Isomer	Yield (%)	M.P.	Lit. M.P. (Ref.)
2'-methyl[a]	75	175-176°	--
3'-methyl[a,b]	80	180-182°	172-174 (9)
4'-methyl[b]	85	214-216°	215-216 (10)

[a] Unreported in the literature.
[b] First isolated during the course of B.Sc. research. See reference 9.

Table 4.
Methylthioxanthones



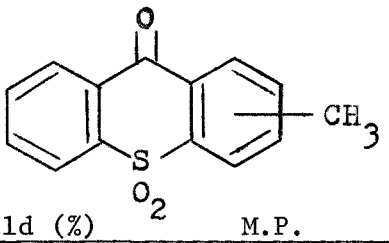
Isomer	Yield (%)	M.P.	Lit. M.P. (Ref.)
1-methyl[a,b]	28	93-95°	--
2-methyl[c]	60	122-124°	123° (11)
3-methyl[a,b,c]	29	115-116°	116-118° (9)
4-methyl[a]	66	146-148°	--

[a] Unreported in the literature.
[b] Individual yield from the separated reaction mixture.
[c] First isolated during the course of B.Sc. research. See reference 9.

Having prepared the thioxanthones, an attempt was made to obtain the corresponding sulfone derivatives. Oxidation of the individual methylthioxanthones with 30% hydrogen peroxide in glacial acetic acid afforded the

expected corresponding thioxanthone 10,10-dioxides. All the reactions proceeded readily and in good yields under the conditions used.

Table 5.
Methylthioxanthone 10,10-dioxides



Isomer	Yield (%)	M.P.	Lit. M.P. (Ref.)
1-methyl[a]	90	201-203°	--
2-methyl	91	204-206°	199° (11)
3-methyl[a]	91	206-207°	--
4-methyl	91	181-182°	172° (12)

[a] Unreported in the literature.

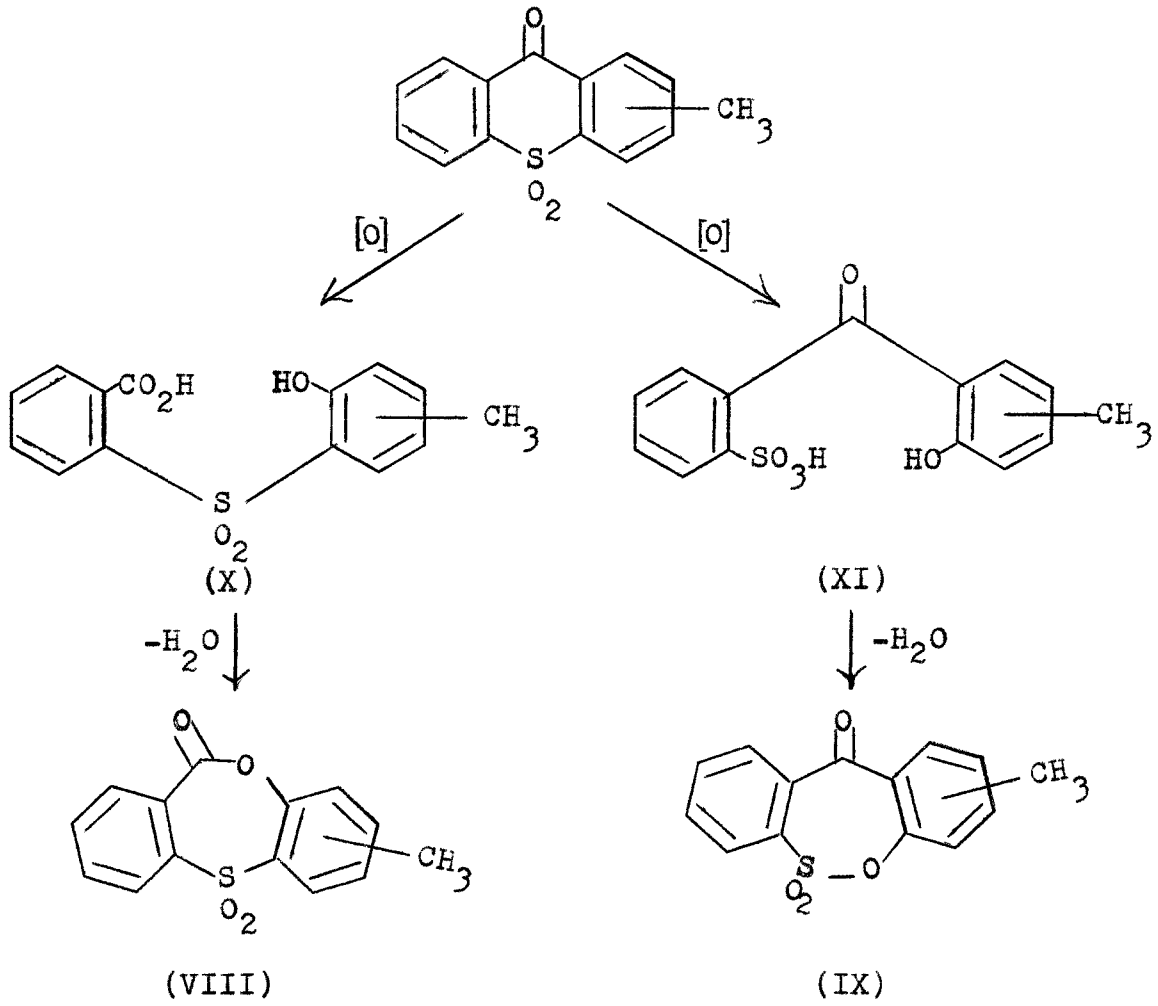
Typically, the oxidation of 2-methylthioxanthone gave a yellow powder with a melting point of 200-202°. A mass spectrum of this material confirmed the formation of the sulfone, but also revealed a minor impurity at m/e 272 and 274 (approximately equal intensities) even after repeated recrystallizations. T.l.c. showed a colorless spot having a large R_f value and a small yellow spot remaining near to the base line. This material was chromatographed to yield 2-methylthioxanthone 10,10-dioxide as white needles melting at 204-206° after crystallization. The mass spectrum of the product showed the presence of no higher molecular weight impurities. A small amount of yellow material adsorbed strongly to the acid-washed alumina column.

When Gilman and Diehl condensed toluene with o-mercaptobenzoic acid, a mixture was obtained which melted over a range of 98-110° even after repeated crystallizations.[13] Oxidation of the material with 30% hydrogen

peroxide in glacial acetic acid gave a 76% yield of 2-methylthioxanthone 10,10-dioxide and a 12% yield of a yellow powder melting at 158.5-160°. Based on infrared data, it was suggested that the latter substance might possibly be 3-methylthioxanthone 10,10-dioxide.

However, when 3-methylthioxanthone was oxidized in the same manner, the usual work-up gave pale yellow needles melting at 200-204°. The mass spectrum of this crude product showed the presence of the sulfone along with the usual minor impurities appearing at m/e 272 and 274. Chromatography of this material gave the expected 3-methylthioxanthone 10,10-dioxide as white needles melting at 206-207° after crystallization, leaving the yellow impurity at the top of the column. Extraction of this yellow band with boiling acetic acid, followed by evaporation to dryness gave a small amount of yellow crystals melting above 300°. Due to the very low ion current in the mass spectrometer and the high melting point of the substance, it was not possible to obtain a mass spectrum, and time did not allow for further study.

Since the ion appearing at m/e 274 is 16 mass units higher than the parent methylthioxanthone 10,10-dioxide $[C_{14}H_{10}SO_3]^{+\cdot}$, at m/e 258, then it is likely that the former ion corresponds to $[C_{14}H_{10}SO_4]^{+\cdot}$. Assuming that this species is due to the incorporation of an oxygen atom into the parent sulfone, then for a given substituted thioxanthone 10,10-dioxide, two isomeric oxidation products are theoretically possible (VIII and IX).



(VIII) (IX)

If the ε-lactone VIII is present, then oxidation of the parent sulfone would have to give rise to the precursor X, which cyclodehydrates, either during the reaction, or later in the mass spectrometer, to yield VIII.

Similarly, oxidation at the SO_2 bridge of the thioxanthone 10,10-dioxide would afford the intermediate sulfonic acid XI, which undergoes elimination of water to form the sultone IX.

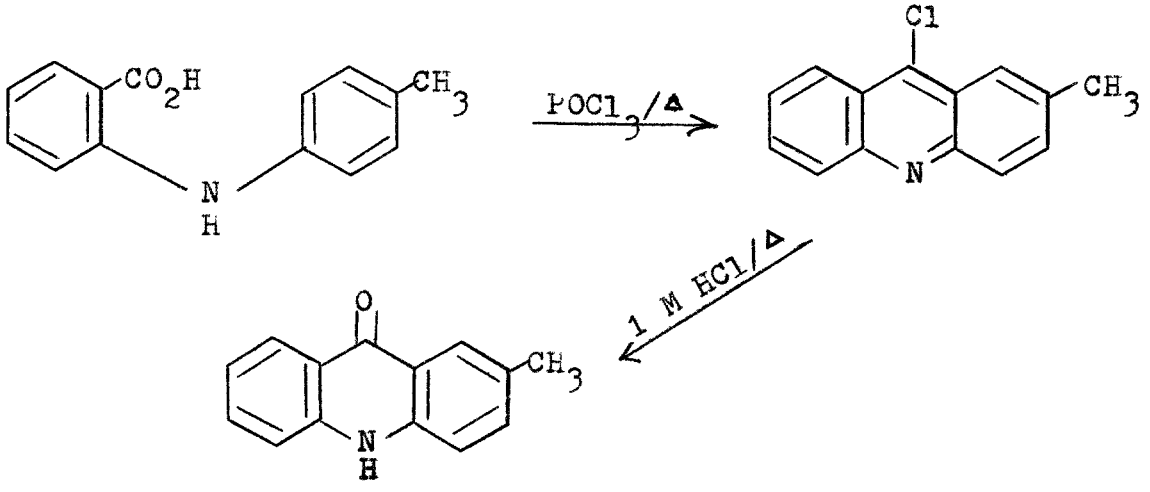
Structures X and XI are in accordance with the chromatographic properties of the yellow impurity, indicating that compound VIII or IX must be elaborated within the mass spectrometer.

There is no apparent formulation for the structure of the ion appearing at m/e 272. Presumably, this corresponds to a separate entity superimposed onto the system.

The N-acylanthranilic acids were obtained from o-chlorobenzoic acid and the aniline in the presence of copper (the Ullmann reaction). The method used by Drozdov[14] to prepare N-p-tolylanthranilic acid is a typical example of the "dry" method originally employed by Ullmann. However, Lehmstedt et al. report best results in preparing the o- and m-tolyl analogues were obtained when using high-boiling amyl alcohol as diluent.[15,16]

Lehmstedt and his co-workers had previously observed that cyclo-dehydration of N-arylanthranilic acids using sulfuric acid was accompanied by simultaneous sulfonation, and that the sulfonate group had to be split off again with hot 30% sulfuric acid.[16]

Better results were obtained by the method in which the 9-chloro-acridines were first obtained in high yields by cyclising appropriate N-arylanthranilic acids with phosphorus oxychloride.[16] Aqueous acid hydrolysed the 9-chloroacridines to the corresponding acridones in good (93-96%) yields.

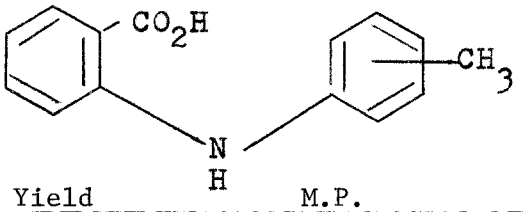


Cyclization of N-m-tolylanthranilic acid provided a mixture of 1- and 3-methyl-9-chloroacridine in approximately a 55:45 ratio (determined by PMR spectra), which does not agree with that reported by Lehmstedt et al.[16] They have reported that a mixture of 9-chloroacridines prepared in an analogous manner underwent aqueous acid hydrolysis to afford firstly a 78% yield of 3-methylacridone followed by 12% of the 1-isomer. The separation was supposedly based upon the differential rates of hydrolysis of the two isomers.

Many attempts to prepare the separated acridones using the foregoing method gave back the starting materials along with a mixture of acridones. Attempts to separate the mixture of 9-chloroacridines using various thin-layer and column chromatographic techniques also failed. Due to the poor solubility in most organic solvents and the similarity in R_f values, the mixture of 1- and 3-methylacridones could not be separated by conventional chromatographic techniques.

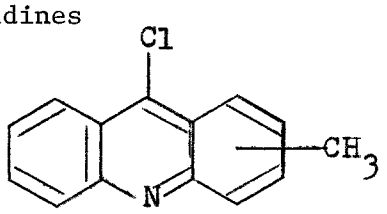
The desired separation was achieved by the method used by Ledochowski et al.[17] Fractional crystallization from benzene of a mixture containing 1- and 3-methyl-9-chloroacridine gave a substantial amount of 1-methyl-9-chloroacridine. The filtrate evaporated to dryness and refluxed with aqueous acid afforded, after 25 minutes, a small amount of analytically pure 3-methylacridone.

Table 6.
N-Tolylanthranilic Acids



Isomer	Yield	M.P.	Lit. M.P. (Ref.)
2'-methyl	69	191-193°	189° (15)
3'-methyl	79	136-137°	137° (16)
4'-methyl	69	200-201°	193-194° (14)

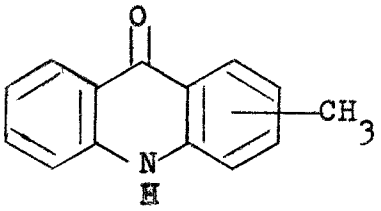
Table 7.
Methyl-9-chloroacridines



Isomer	Yield (%)	M.P.	Lit. M.P. (Ref.)
1-methyl	33[a]	94-95°	93-95° (17)
2-methyl	88	116-118°	117-118° (14)
3-methyl	--	--	118-119.5° (17)
4-methyl	90	88-90°	96-97° (18)

[a] Obtained from the mixture of 1- and 3-methyl isomers.

Table 8.
Methylacridones

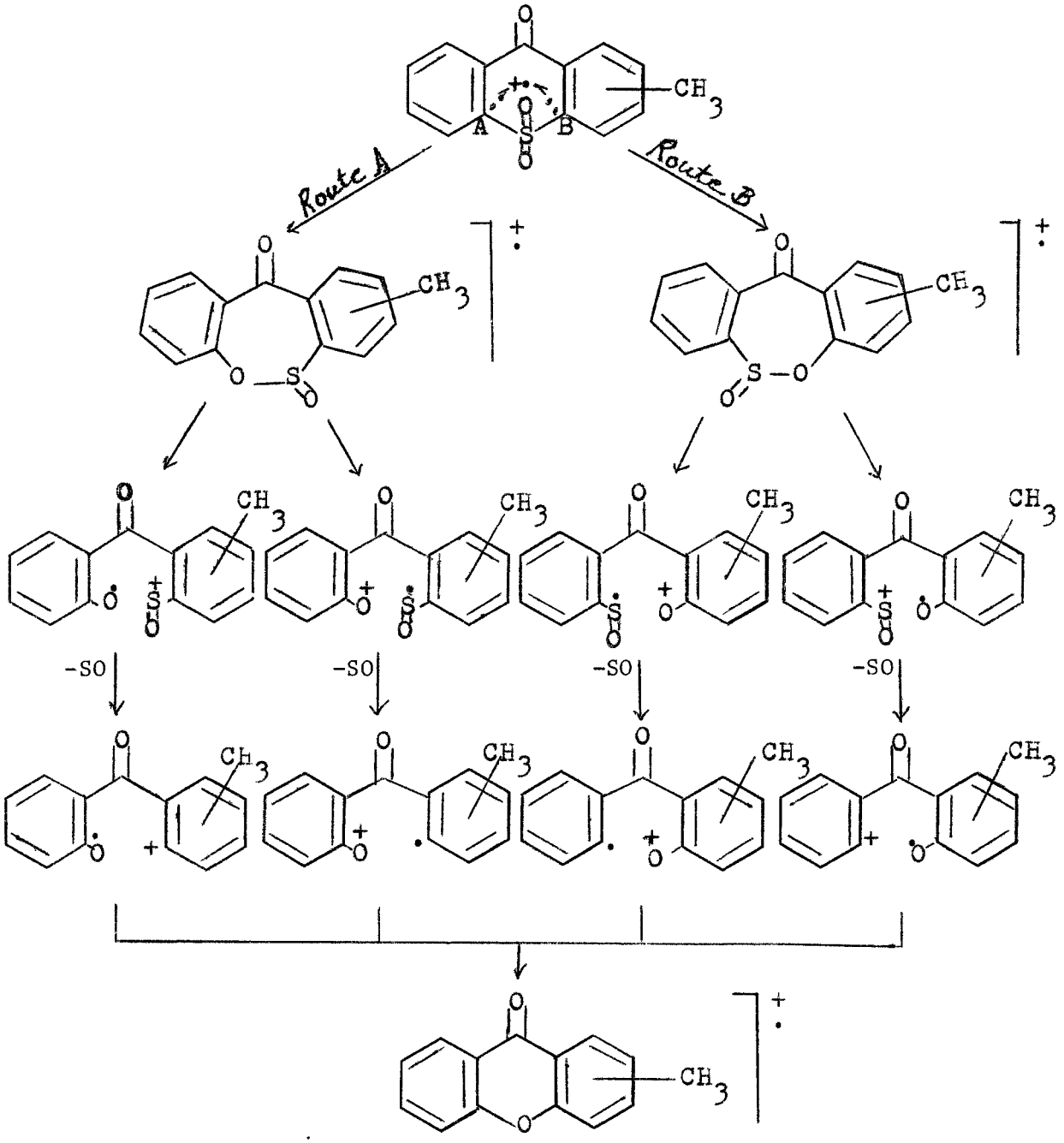


Isomer	Yield (%)	M.P.	Lit. M.P. (Ref.)
1-methyl	78	322-325°	318° (18)
2-methyl	96	320-323°	338° (19)
3-methyl	6[a]	337-340°	332-335° (17)
4-methyl	93	333-335°	345-346° (20)

[a] Starting from the mixture of 1- and 3-methyl-9-chloroacridines.

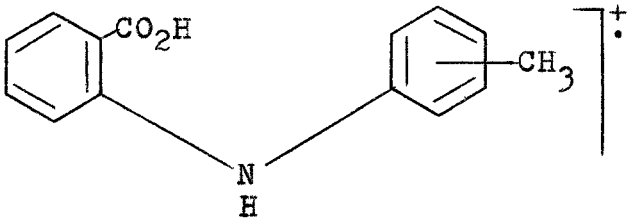
2.2 Electron Impact Induced Fragmentations

The base peak in the mass spectra of 2-, 3- and 4-methylthioxanthone 10,10-dioxide corresponds to the elimination of SO, probably through aryl group migration, leaving a xanthone product. Diaryl sulfones with different aryl substituents can undergo migration of either aryl group, as indicated by routes A and B.[21]



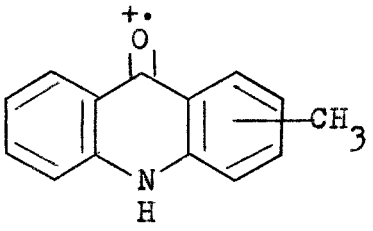
Migration of an aryl group suggests that the electron deficiency is largely localized in a non-bonding oxygen orbital of the sulfone, and hence an aryl group better able to function as an electron donor should preferentially migrate. Meyerson and co-workers have demonstrated that migratory aptitude apparently increases with increasing substitution of the phenyl group by electron-donating methyl groups.[22]

The fragmentation of N-tolylanthranilic acids is dominated by the facile elimination of water, probably through cyclodehydration. This is followed by $H^{\bullet}$ loss and then subsequent acridone fragmentation by expulsion of 28 mass units.



227

$-H_2O$



209

$-H^{\bullet}$

$[C_{14}H_{10}NO]^+$

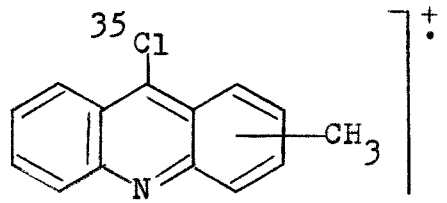
208

$-CO$

$[C_{13}H_{10}N]^+$

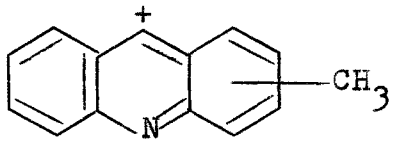
180

Methyl-9-chloroacridines preferentially expel $Cl^{\bullet}$ to afford the major $[M-Cl^{\bullet}]^{+}$ ion. This is followed by $H^{\bullet}$ loss and then subsequent methylacridine fragmentation by expulsion of 26 or 27 mass units.



227

$-.Cl$



192

$-H^{\bullet}$

$[C_{14}H_9N]^{+\cdot}$

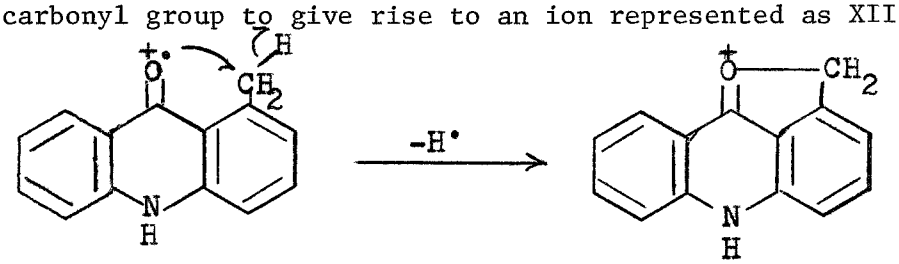
191

$-CN^{\bullet}$

$[C_{13}H_9]^{+}$

165

The $[M-H^{\bullet}]^{+}$ ion is much more intense in the methylacridones than in the corresponding 9-chloroacridines, implying some N-H fission. However, the observation that 1-methylacridone again shows by far the strongest loss of $H^{\bullet}$ could also imply that C-H fission is encouraged by interaction with the carbonyl group to give rise to an ion represented as XII.[23]



(XII)

2.3 Proton Magnetic Resonance Spectra

Fig. 1

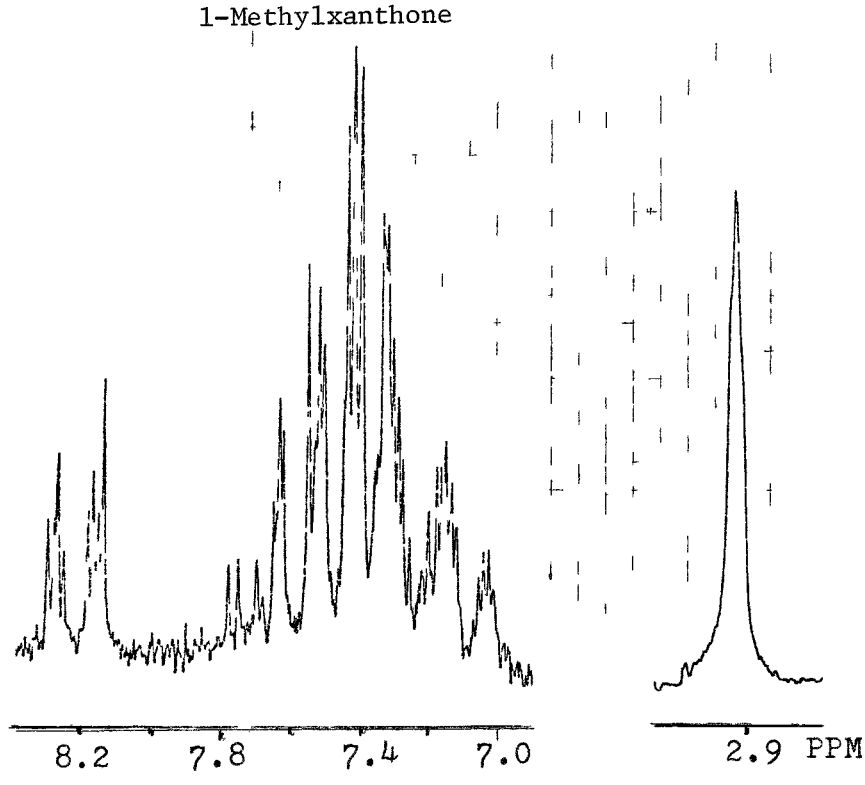


Fig. 1. 60 MHz proton spectrum in $CDCl_3$.

Fig. 2

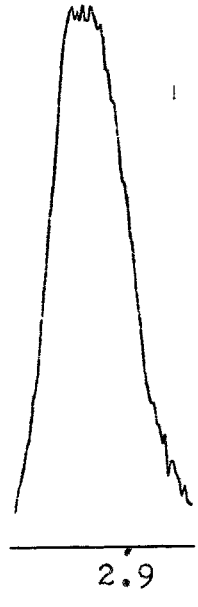


Fig. 3

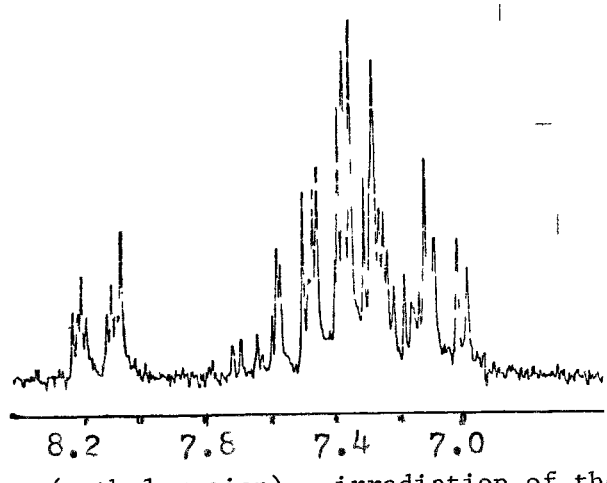


Fig. 2. Double resonance spectrum (methyl region), irradiation of the high field aromatic (ν_2 = 439.3 Hz) couplings ca. 0.2 Hz.
Fig. 3. Double resonance spectrum (aromatic region), irradiation of the methyl protons, ν_2 = 175.2 Hz.

Fig. 4.

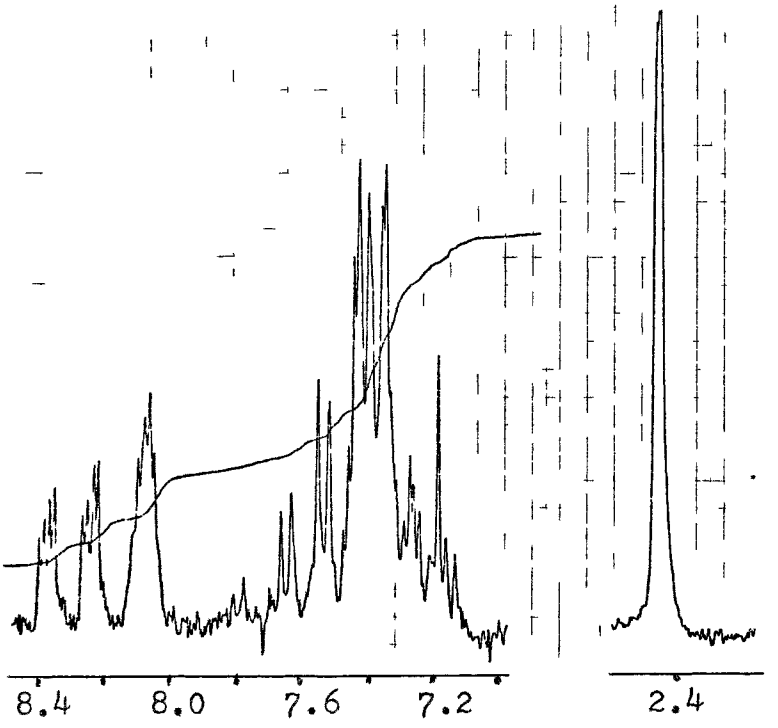


Fig. 4. 60 MHz proton spectrum of 2-methylxanthone in $CDCl_3$.

Fig. 5. Double resonance spectrum (aromatic region) of 2-methylxanthone, irradiation of the methyl protons, ν_2 = 145.9 Hz.

Fig. 5.

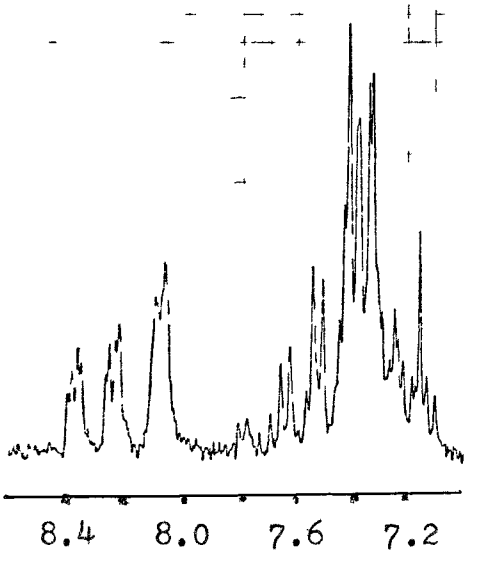


Fig. 6

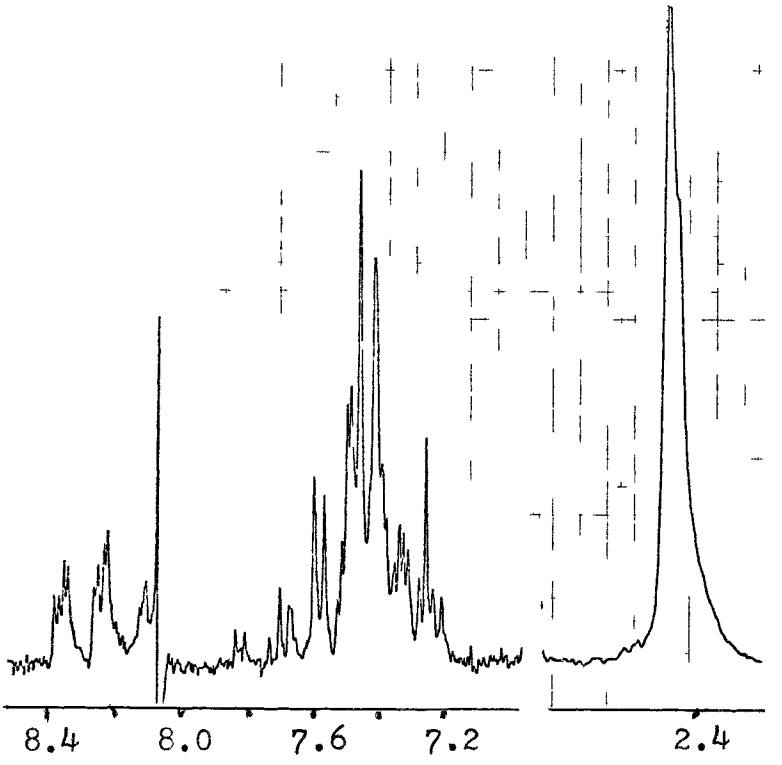


Fig. 6. Double resonance spectrum of 2-methylxanthone, irradiation of H-1 (ν_2 ca. 484 Hz).

Fig. 7.

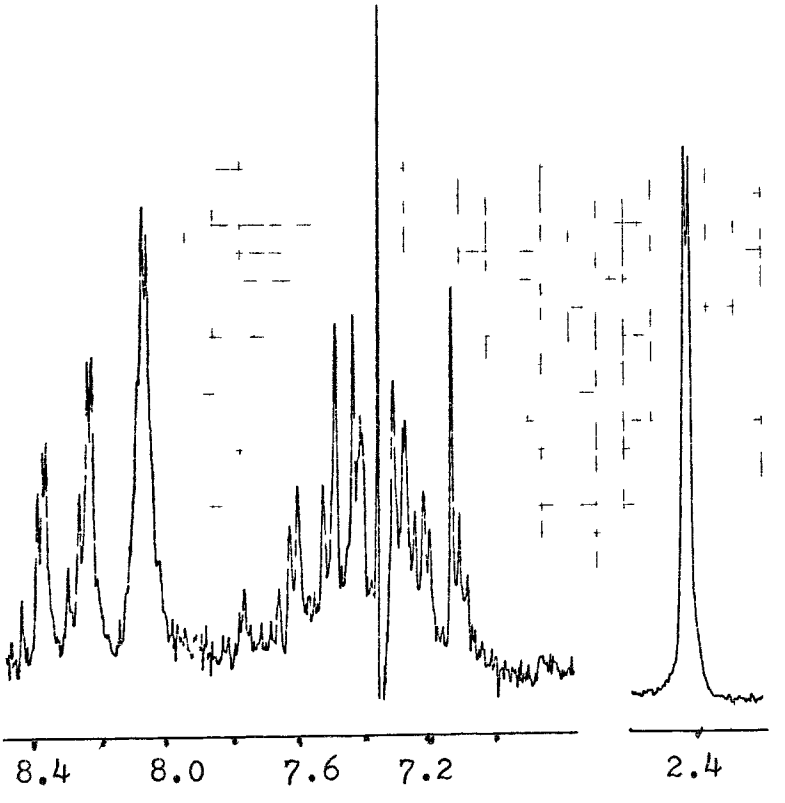


Fig. 7. Double resonance spectrum of 2-methylxanthone, irradiation of mid-field aromatic (ν_2 = 433.5 Hz). Methyl coupling 0.55 Hz.

Fig. 8

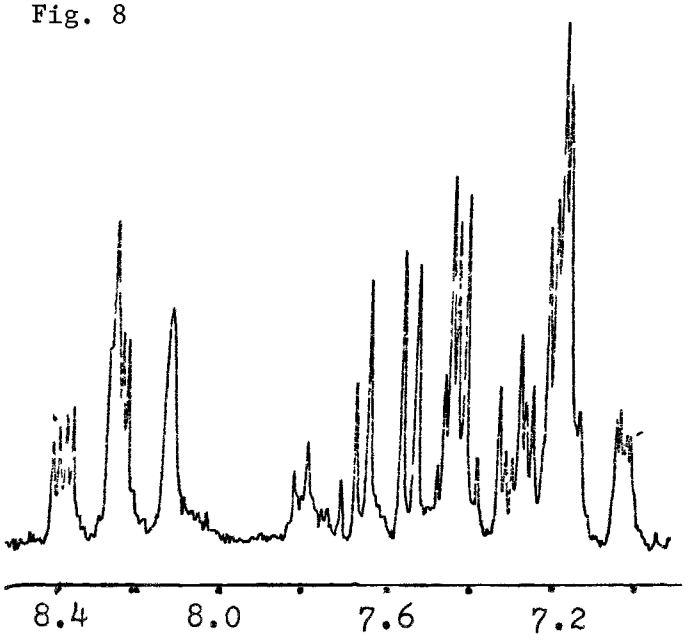


Fig. 9

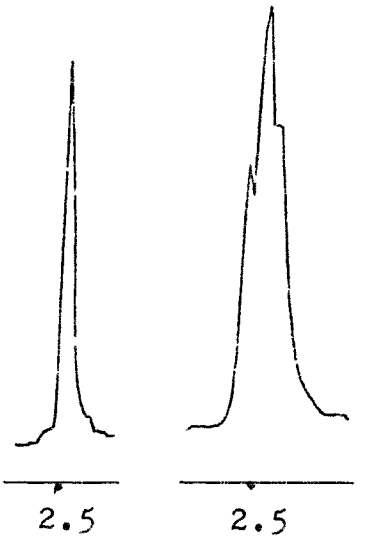


Fig. 8. 60 MHz proton spectrum of 3-methylxanthone in $CDCl_3$.

Fig. 9. Double resonance spectrum (methyl region) of 3-methylxanthone, irradiation of H-1 proton, ν_2 ca. 489 Hz.

Fig. 10. Double resonance spectrum (aromatic region) of 3-methylxanthone, irradiation of the methyl protons, ν_2 = 149.2.

Fig. 11. Double resonance spectrum of 3-methylxanthone, irradiation of high field aromatic proton, ν_2 = 452.5 Hz. Methyl coupling 0.55 Hz.

Fig. 11.

Fig. 10

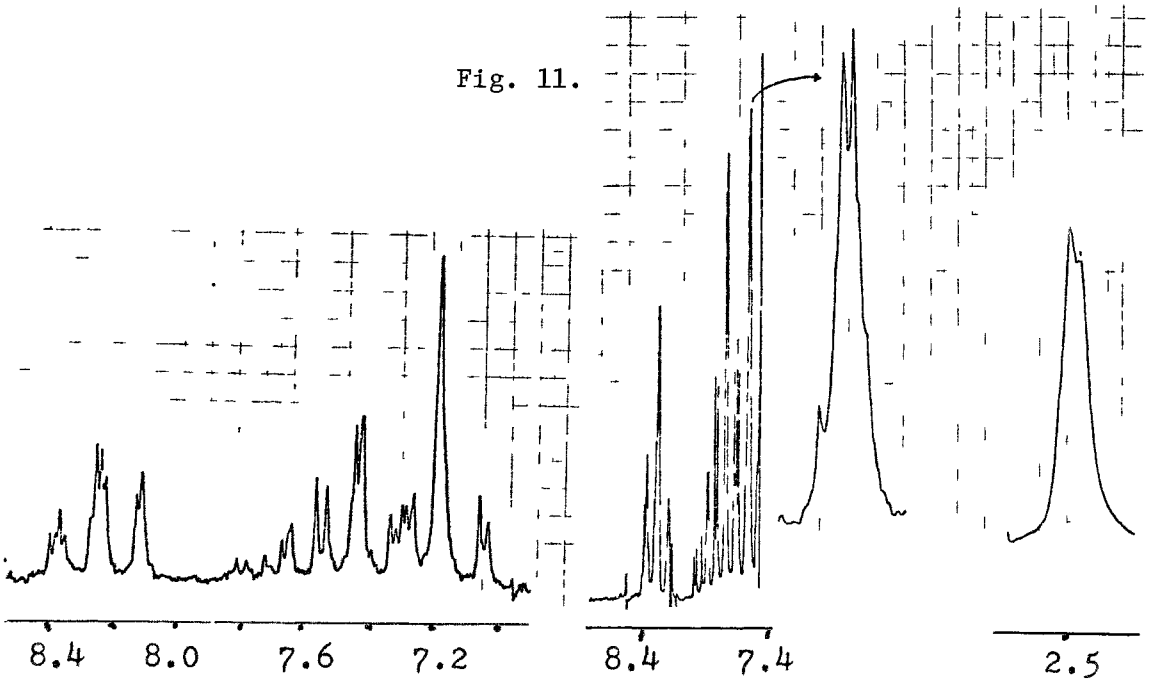


Fig. 12. 60 MHz proton spectrum (aromatic region) of 4-methylxanthone in $CDCl_3$.

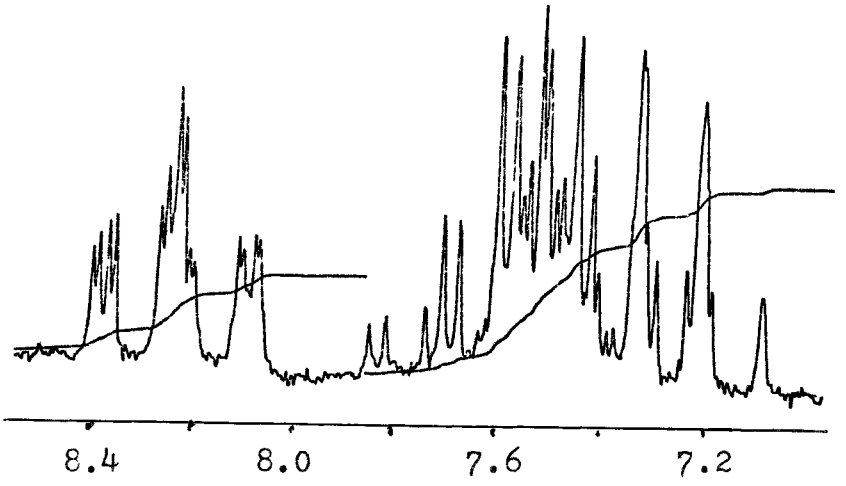


Fig. 13. Double resonance spectrum (aromatic region) of 4-methylxanthone, irradiation of the methyl protons, ν_2 = 153.0 Hz.

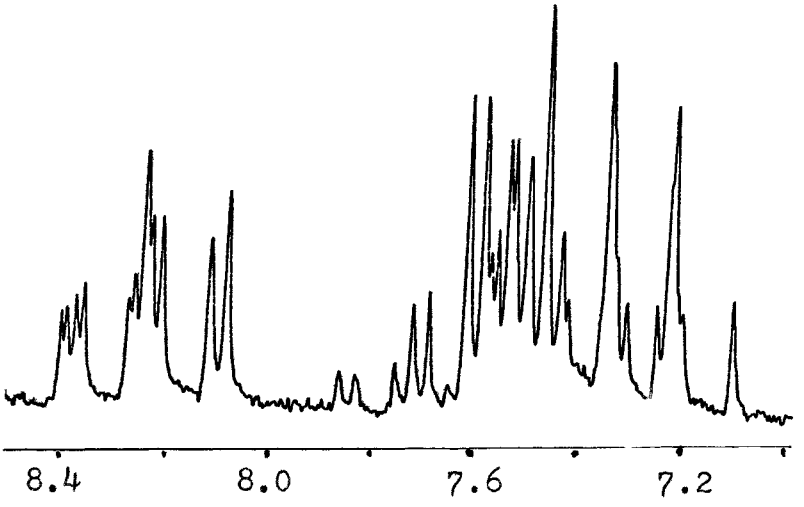


Fig. 14. Double resonance spectrum of 4-methylxanthone, irradiation of H-1, ν_2 = 493.3 Hz. Methyl coupling 0.55 Hz.

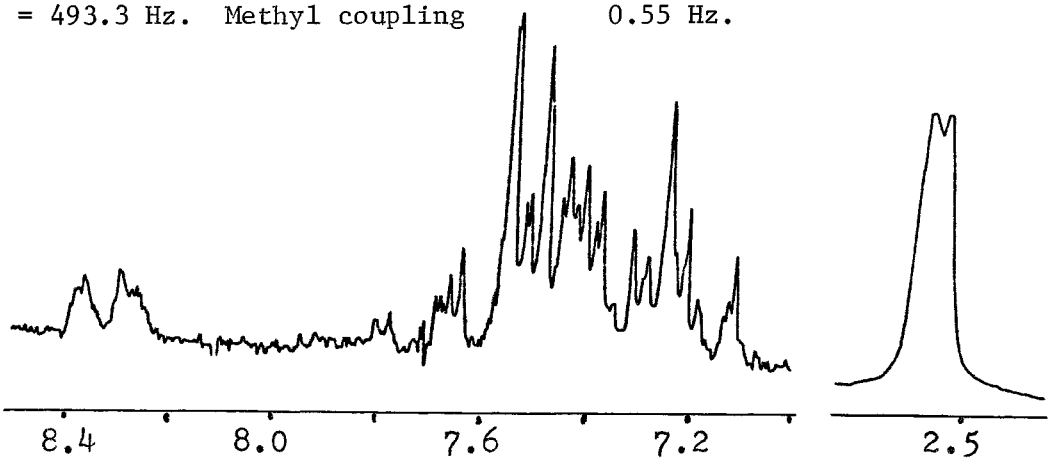


Fig. 15

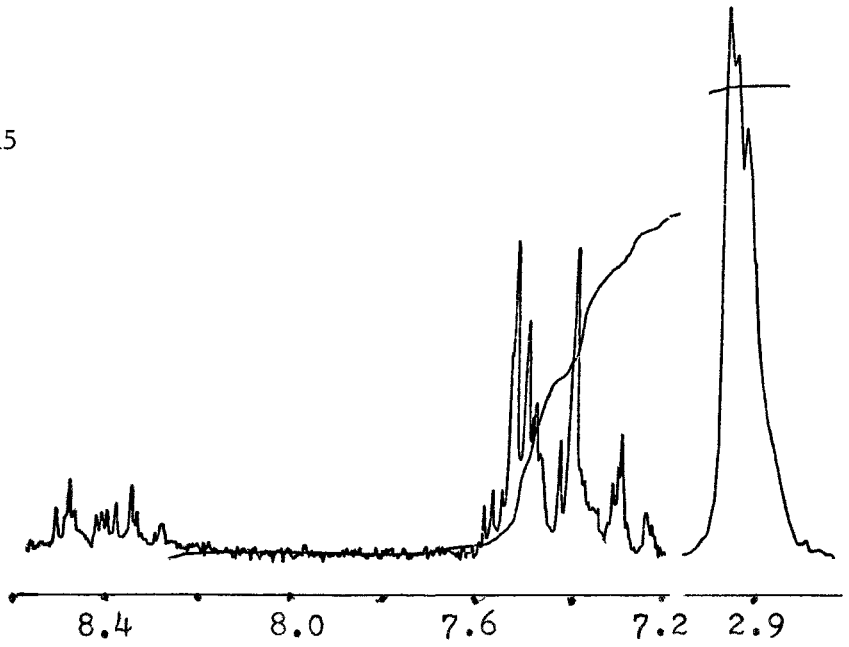


Fig. 15. 60 MHz spectrum of 1-methylthioxanthone in $CDCl_3$.

Fig. 16. Double resonance spectra of 1-methylthioxanthone (aromatic region) irradiation of the methyl protons, ν_2 = 174.6 Hz. (Methyl region) irradiation of the high field aromatic, line width = 0.7 Hz.

Fig. 16.

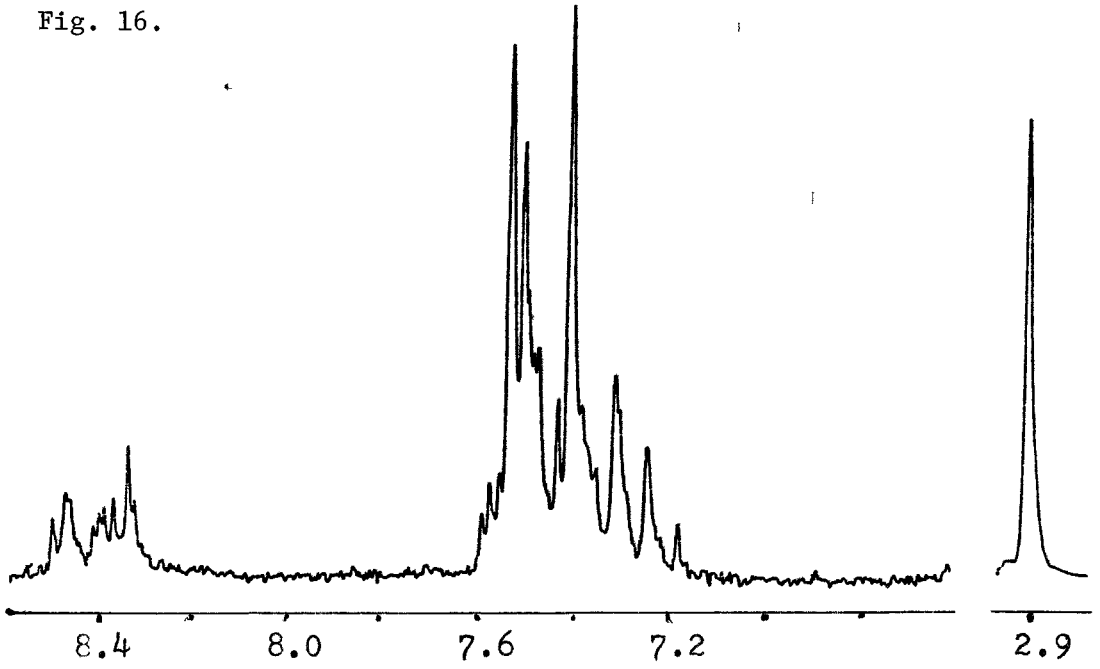


Fig. 17.

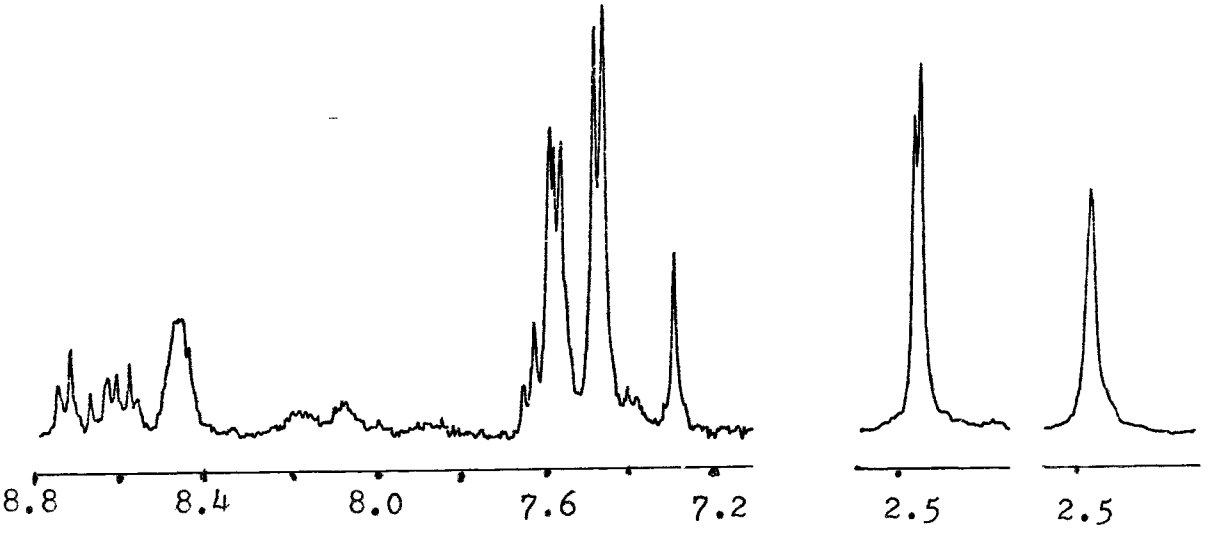


Fig. 17. 60 MHz proton spectrum of 2-methylthioxanthone in $CDCl_3$, methyl coupling = 0.73 Hz. Double resonance spectrum (right methyl region), irradiation of H-1, ν_2 ca. 504 Hz.

Fig. 18.

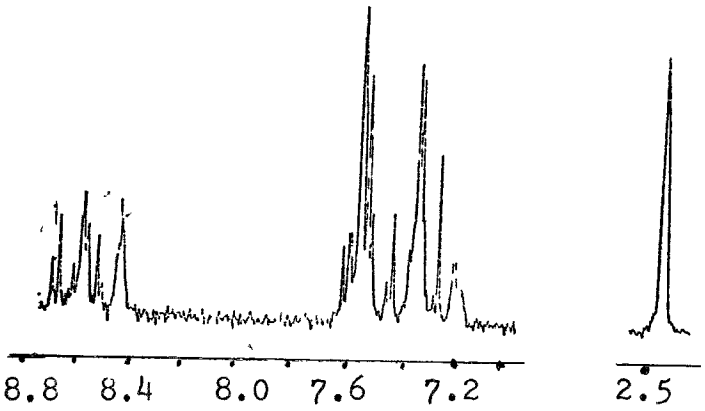


Fig. 18. 60 MHz proton spectrum of 3-methylthioxanthone in $CDCl_3$.

Fig. 19.

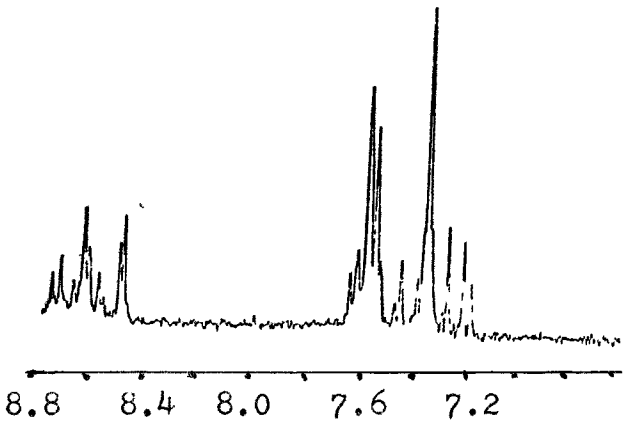


Fig. 19. Double resonance spectrum (aromatic region) of 3-methylthioxanthone, irradiation of the methyl protons, ν_2 = 147.7 Hz.

Fig. 20.

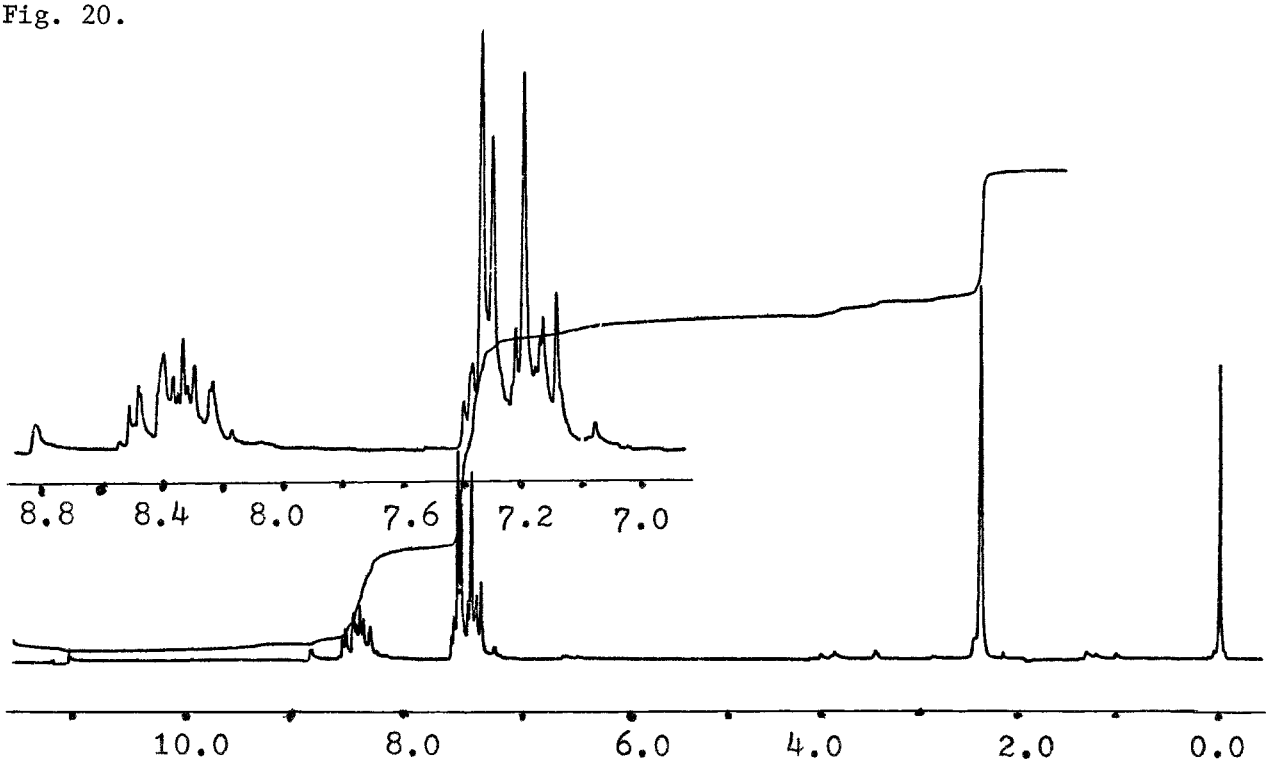


Fig. 20. 60 MHz proton spectrum of 4-methylthioxanthone in $CDCl_3$.

Fig. 21. Double resonance spectrum of 4-methylthioxanthone, irradiation of the high field aromatic proton (arrow). Methyl line width ca. 0.75 Hz.

Fig. 21.

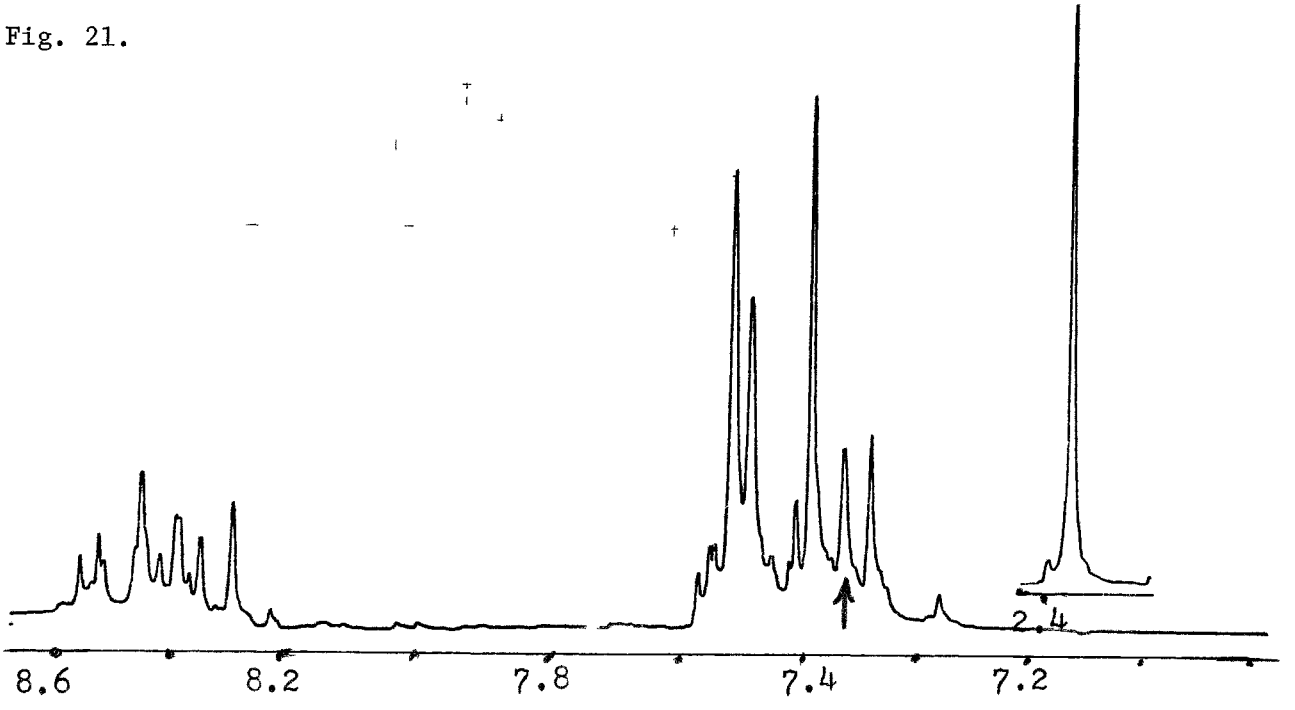


Fig. 22

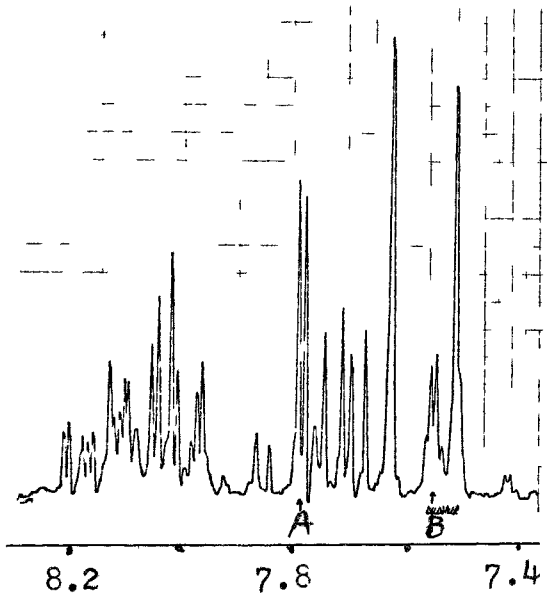


Fig. 22. 60 MHz proton spectrum (aromatic region) of 1-methylthioxanthone 10,10-dioxide in $CDCl_3$.

Fig. 23. Double resonance spectrum (aromatic region) of 1-methylthioxanthone 10,10-dioxide, irradiation of the methyl protons, ν_2 = 164.6 Hz.

Fig. 23.

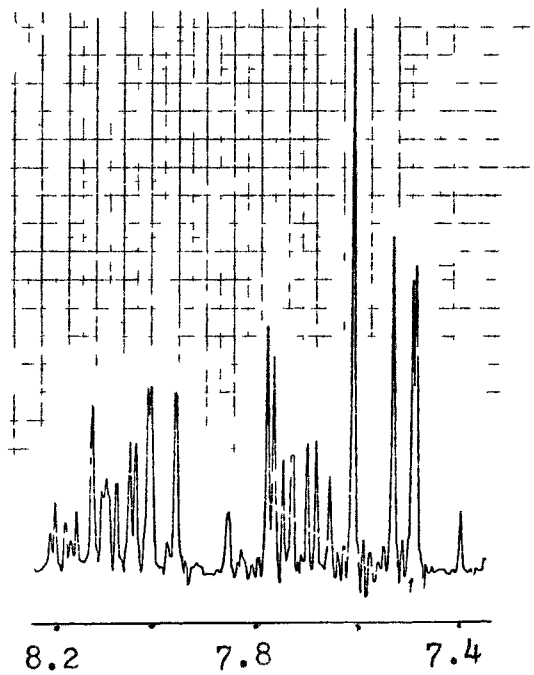


Fig. 24.

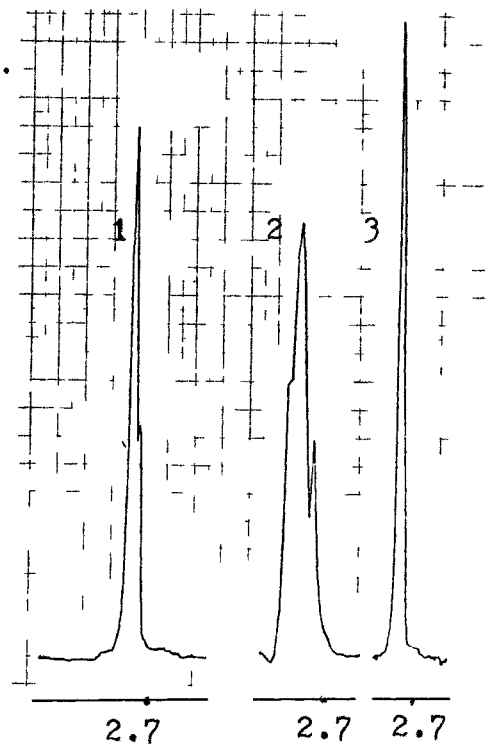


Fig. 24. Double resonance spectra (methyl region) of 1-methylthioxanthone 10,10-dioxide; 1. irradiation at B (ν_2 = 456.6 Hz) (cf. Fig. 22). 2. Plot expansion of 1. and 3. irradiation at A (ν_2 = 470.0 Hz).

Fig. 25. 60 MHz proton spectrum of 2-methylthioxanthone 10,10-dioxide in $CDCl_3$.

Fig. 25.

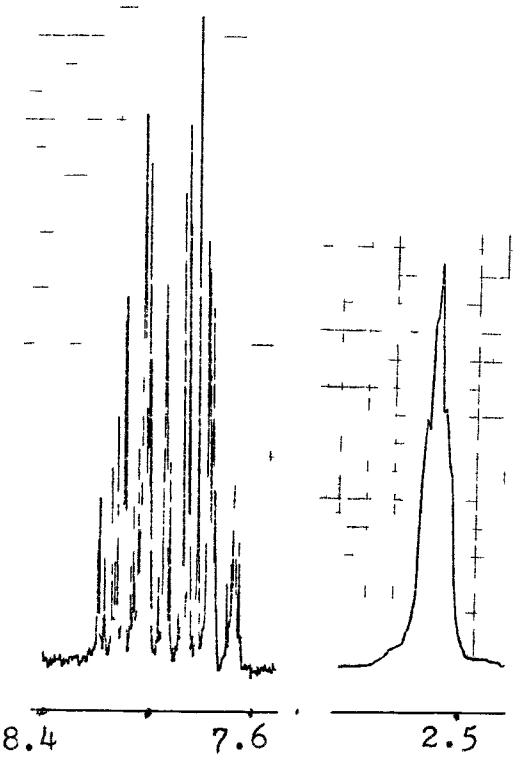


Fig. 26. Double resonance spectrum (aromatic region) of 2-methylthioxanthone 10,10-dioxide, irradiation of the methyl protons, ν_2 = 151.6 Hz.

Fig. 26

Fig. 27

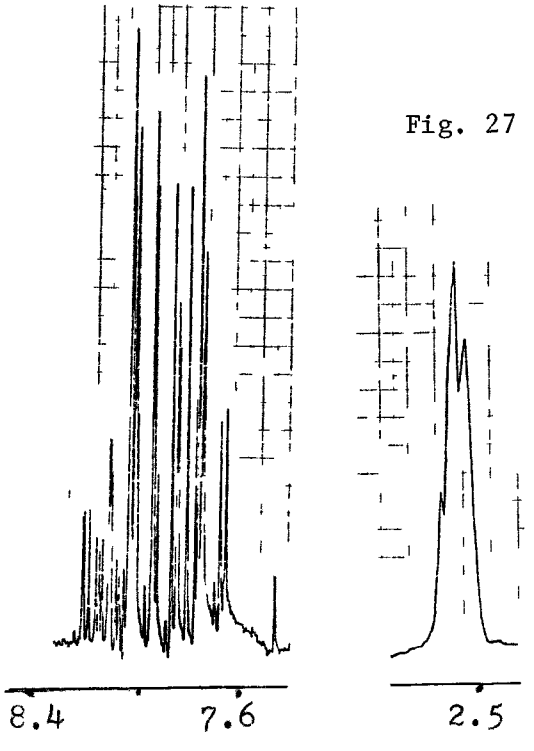


Fig. 27. Double resonance spectrum (methyl region) of 2-methylthioxanthone 10,10-dioxide, irradiation of the high field aromatic proton, ν_2 = 455.3 Hz. Large methyl coupling = 0.55 Hz.

Fig. 28. 60 MHz proton spectrum (aromatic region) of 3-methylthioxanthone 10,10-dioxide in $CDCl_3$.

Fig. 28.

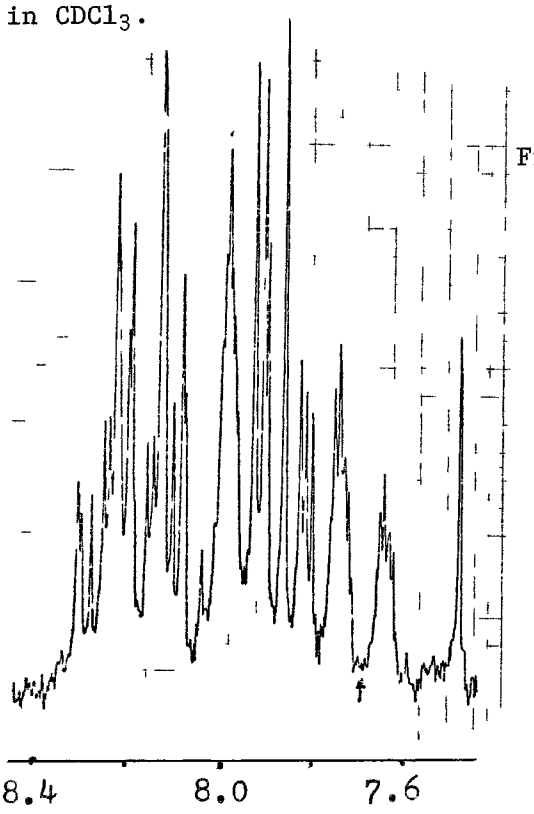


Fig. 29.

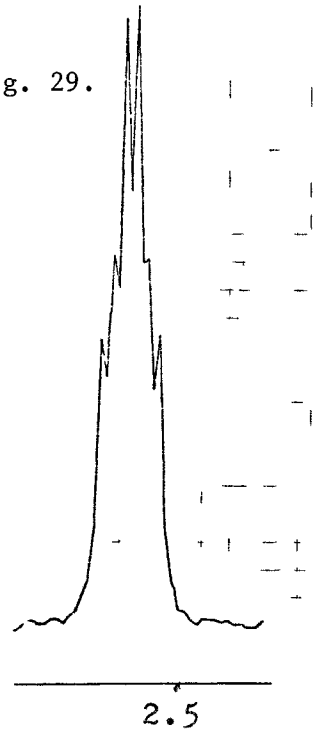


Fig. 29. 60 MHz proton spectrum (methyl region) of 3-methylthioxanthone 10,10-dioxide.

Fig. 30. Double resonance spectrum (aromatic region) of 3-methylthioxanthone 10,10-dioxide, irradiation of the methyl protons, ν_2 = 153.3 Hz.

Fig. 30.

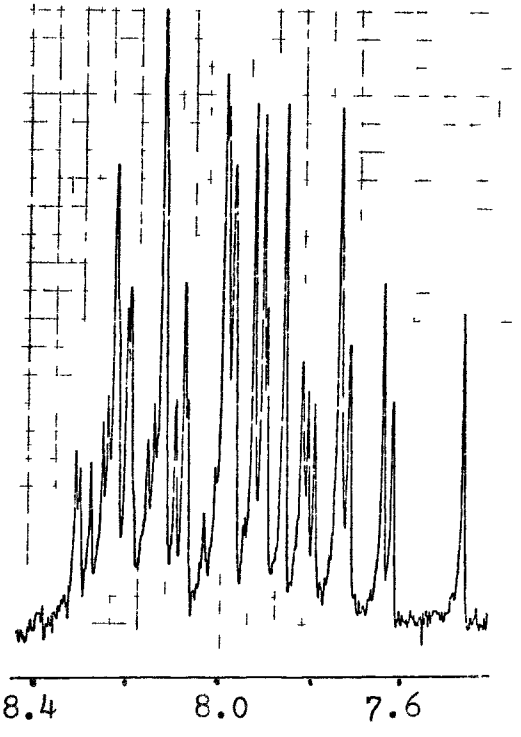


Fig. 31.

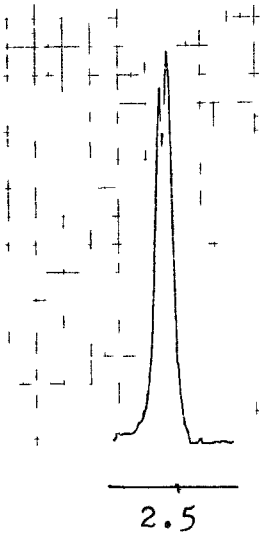


Fig. 31. Double resonance spectrum (methyl region) of 3-methylthioxanthone 10,10-dioxide, irradiation at the centre of the two high field aromatic multiplets. Methyl coupling = 0.55 Hz.

Fig. 32

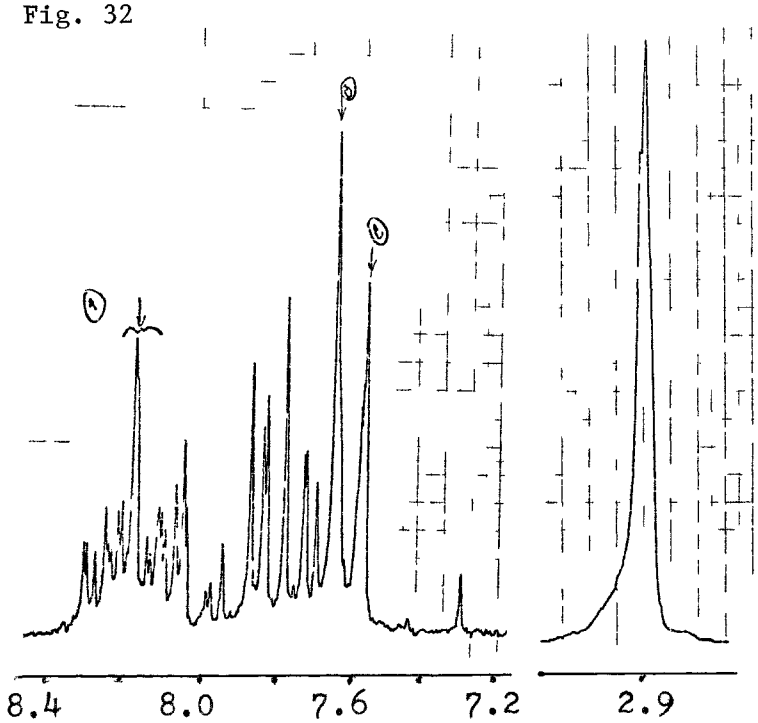


Fig. 33.

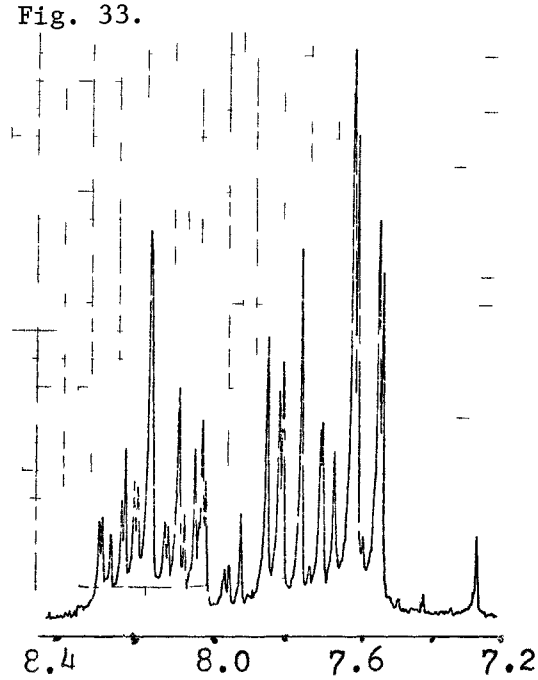


Fig. 32. 60 MHz proton spectrum of 4-methylthioxanthone 10,10-dioxide in $CDCl_3$.

Fig. 33. Double resonance spectrum (aromatic region) of 4-methylthioxanthone 10,10-dioxide, irradiation of the methyl protons, ν_2 = 174.0 Hz.

Fig. 34.

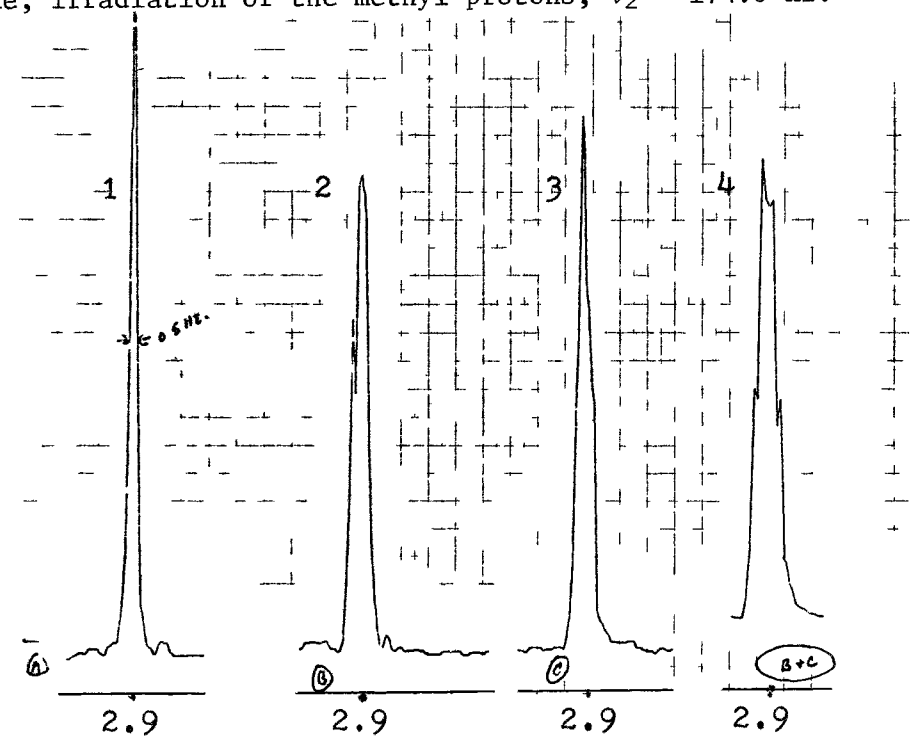


Fig. 34. Double resonance spectrum (methyl region) of 4-methylthioxanthone 10,10-dioxide, 1. irradiation at A (cf. Fig. 32) take the line width to 0.55 Hz, 2. irradiation at B, 3. irradiation at C, and 4. irradiation at B and C.

Fig. 35.

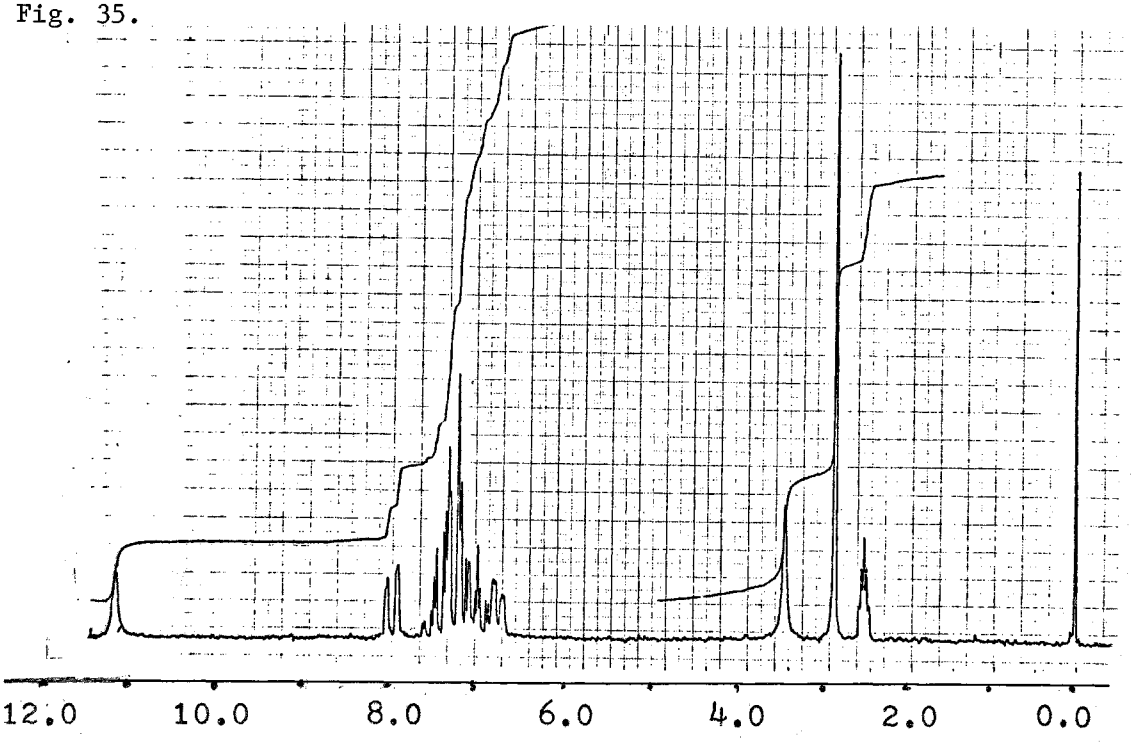


Fig. 35. 60 MHz proton spectrum of 1-methylacridone in DMSO-d_6.

Fig. 36. 60 MHz proton spectrum (aromatic region) of 1-methylacridone.

Fig. 36

Fig. 37.

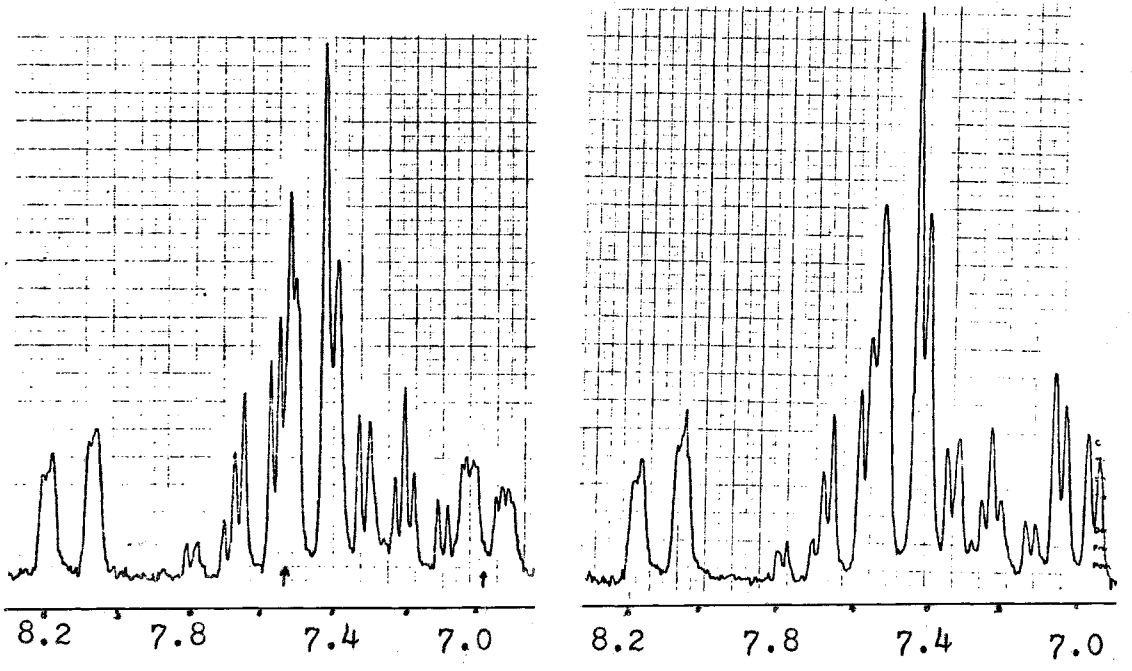


Fig. 37. Double resonance spectrum (aromatic region) of 1-methylacridone, irradiation of the methyl protons, ν_2 = 173.6 Hz.

Fig. 38.

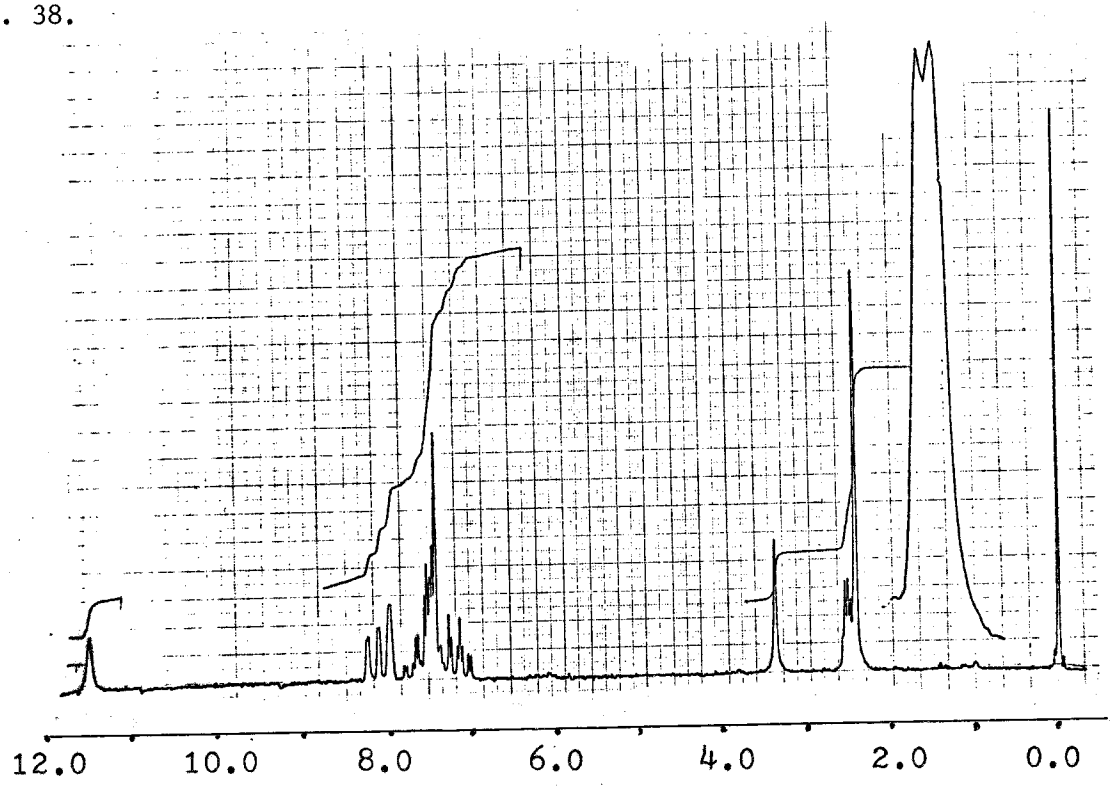


Fig. 38. 60 MHz proton spectrum of 2-methylacridone in DMSO-d_6. Plot expansion of the methyl gives J = 0.73 Hz.

Fig. 39. 60 MHz proton spectrum (aromatic region) of 2-methylacridone.

Fig. 39

Fig. 40

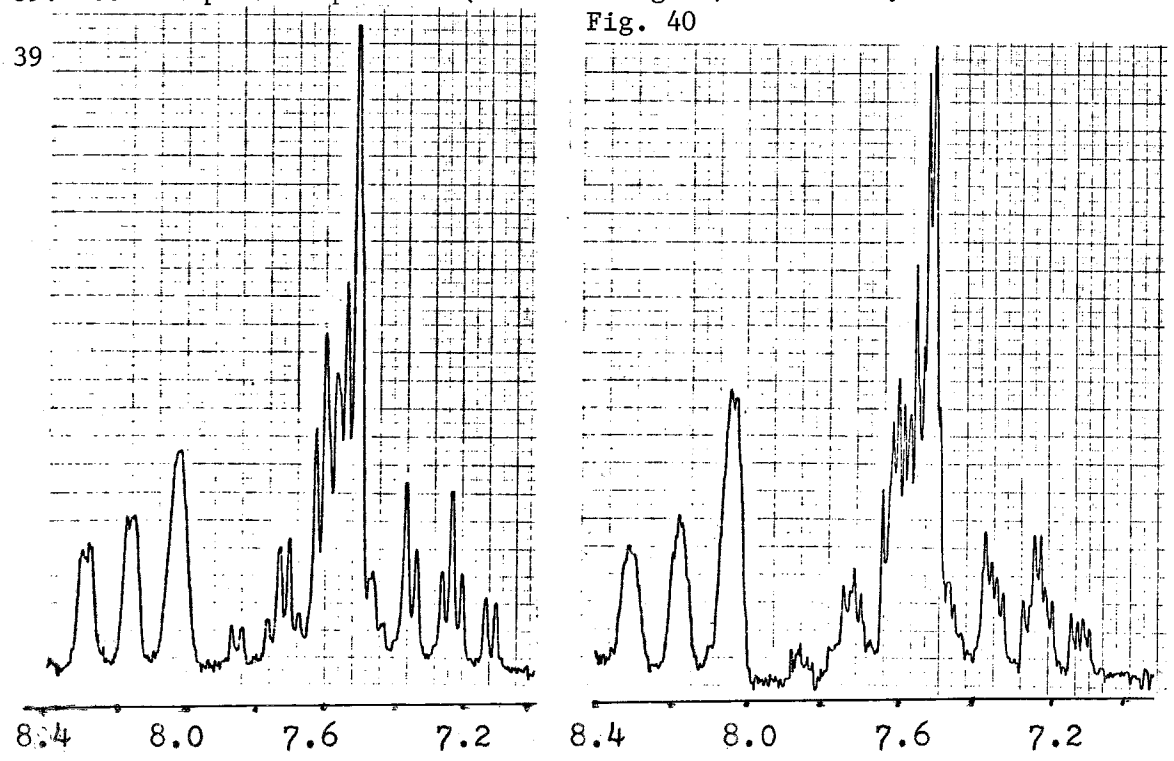


Fig. 40. Double resonance spectrum (aromatic region) of 2-methylacridone, irradiation of the methyl protons (ν_2 = 145.8 Hz).

Fig. 41. 60 MHz proton spectrum of 3-methylacridone in DMSO-d_6.

Fig. 41.

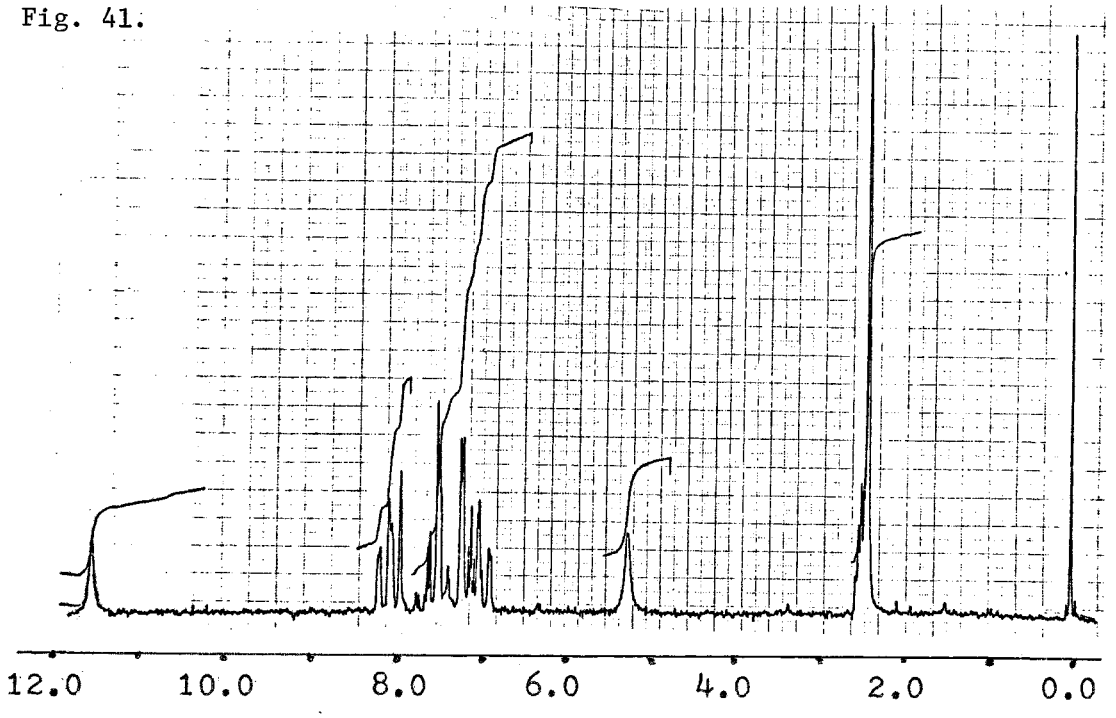


Fig. 42. 60 MHz proton spectrum (aromatic region) of 3-methylacridone.

Fig. 43. Double resonance spectrum (aromatic region) of 3-methylacridone, irradiation at the methyl protons (ν_2 = 147.6 Hz).

Fig. 42.

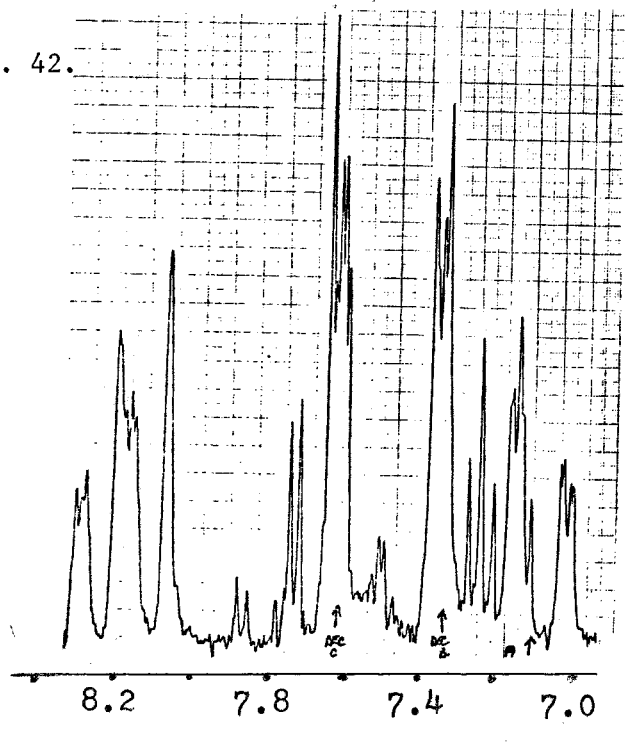


Fig. 43.

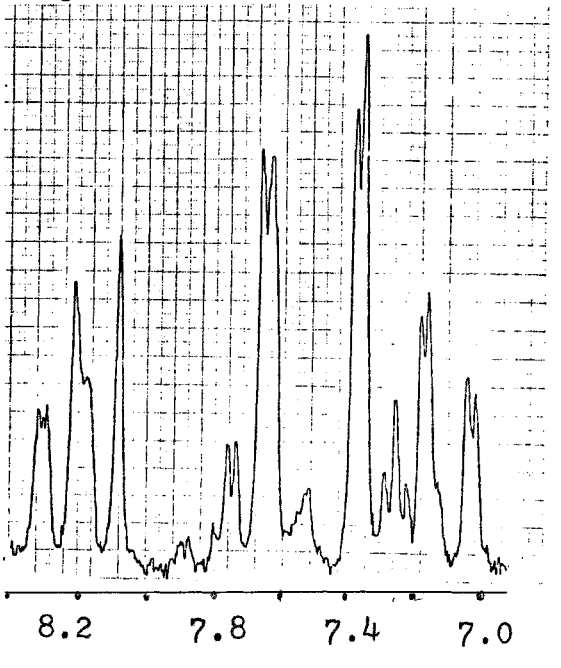


Fig. 44.

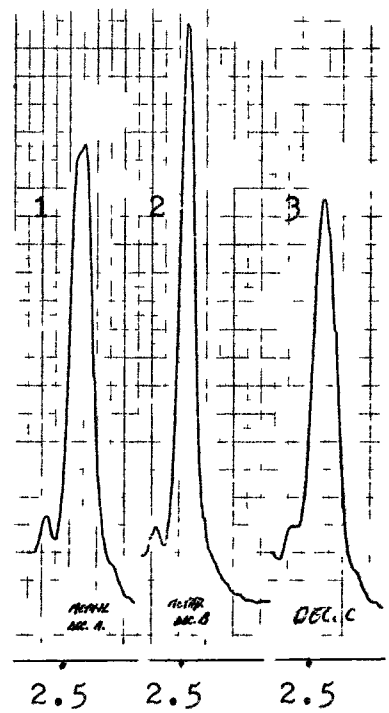


Fig. 44. Double resonance spectra (methyl region) of 3-methylacridone, 1. irradiation at A (cf. Fig. 43), 2. irradiation at B and 3. irradiation at C.

Fig. 45. 60 MHz proton spectrum of 4-methylacridone in DMSO-d_6.

Fig. 45.

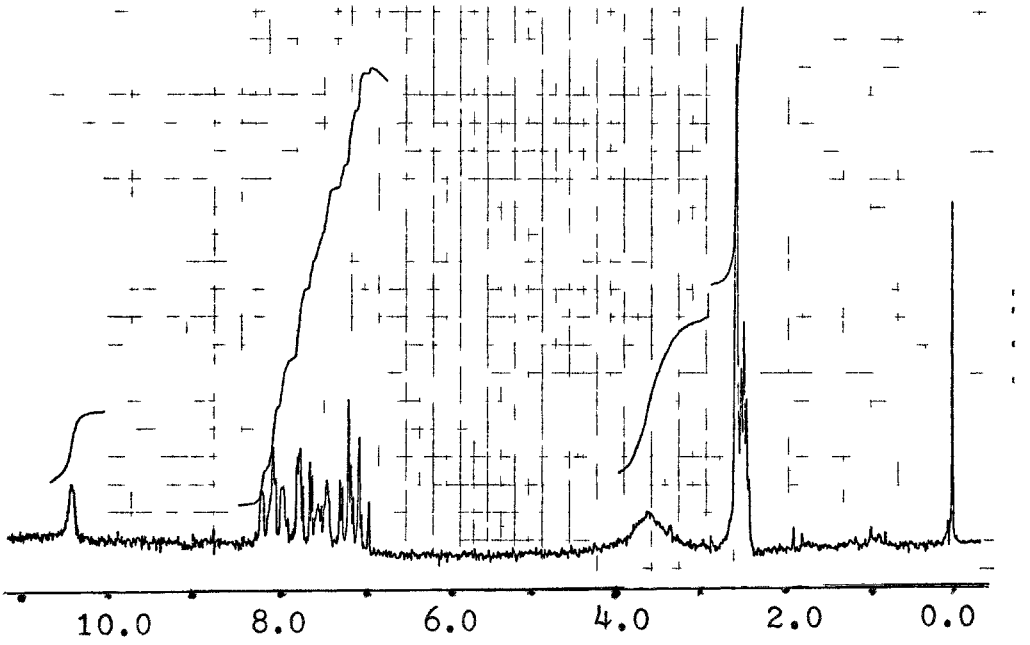


Fig. 46. 60 MHz proton spectrum (aromatic region) of 4-methylacridone.

Fig. 47. Double resonance spectrum (aromatic region) of 4-methylacridone, irradiation of the methyl protons (ν_2 = 156.2 Hz).

Fig. 46.

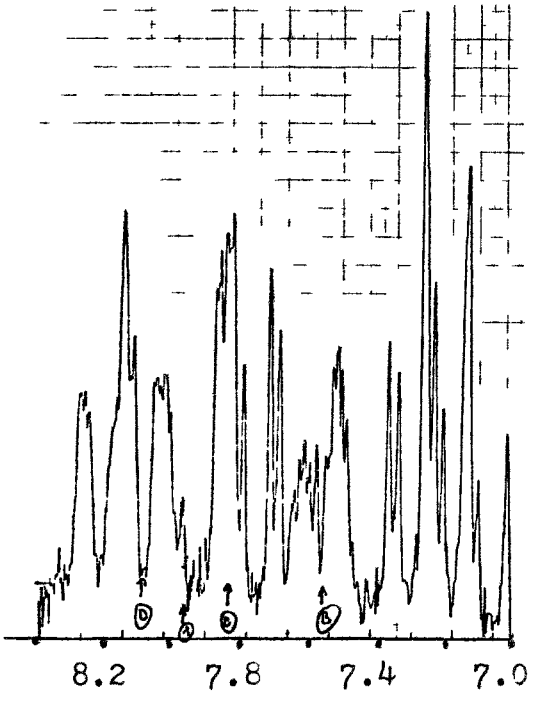


Fig. 47

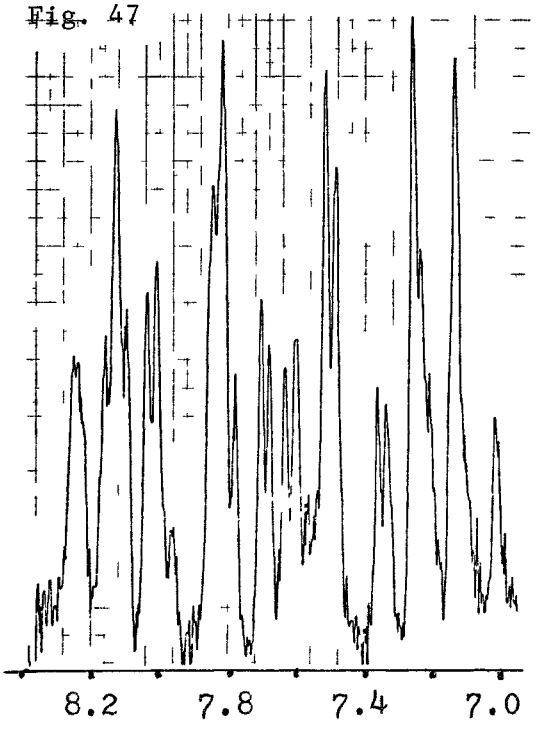


Fig. 48.

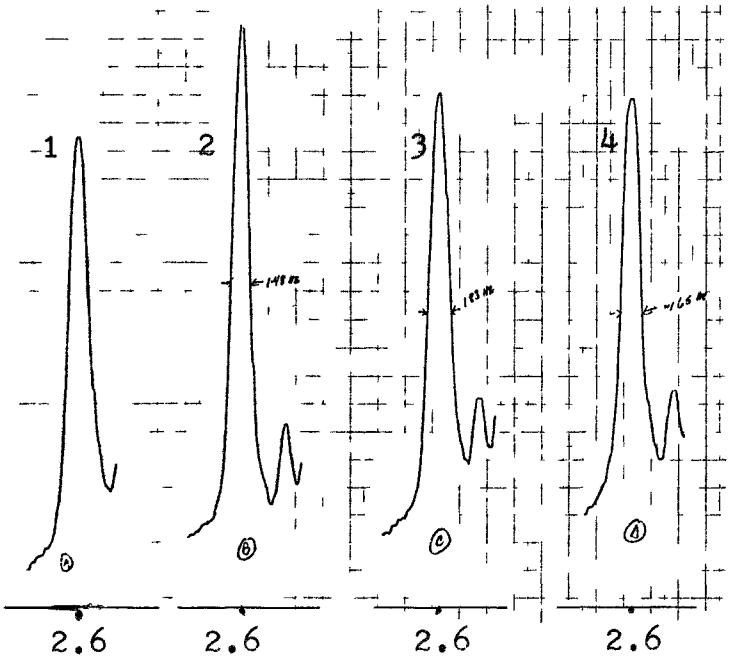


Fig. 48. Double resonance spectra (methyl region) of 4-methylacridone, 1. irradiation at A (cf. Fig. 46), 2. irradiation at B, 3. irradiation at C and 4. irradiation at D.

Fig. 49. 60 MHz proton spectrum of 1-methyl-9-chloroacridine in $CDCl_3$. The large aromatic signal is due to benzene.

Fig. 49.

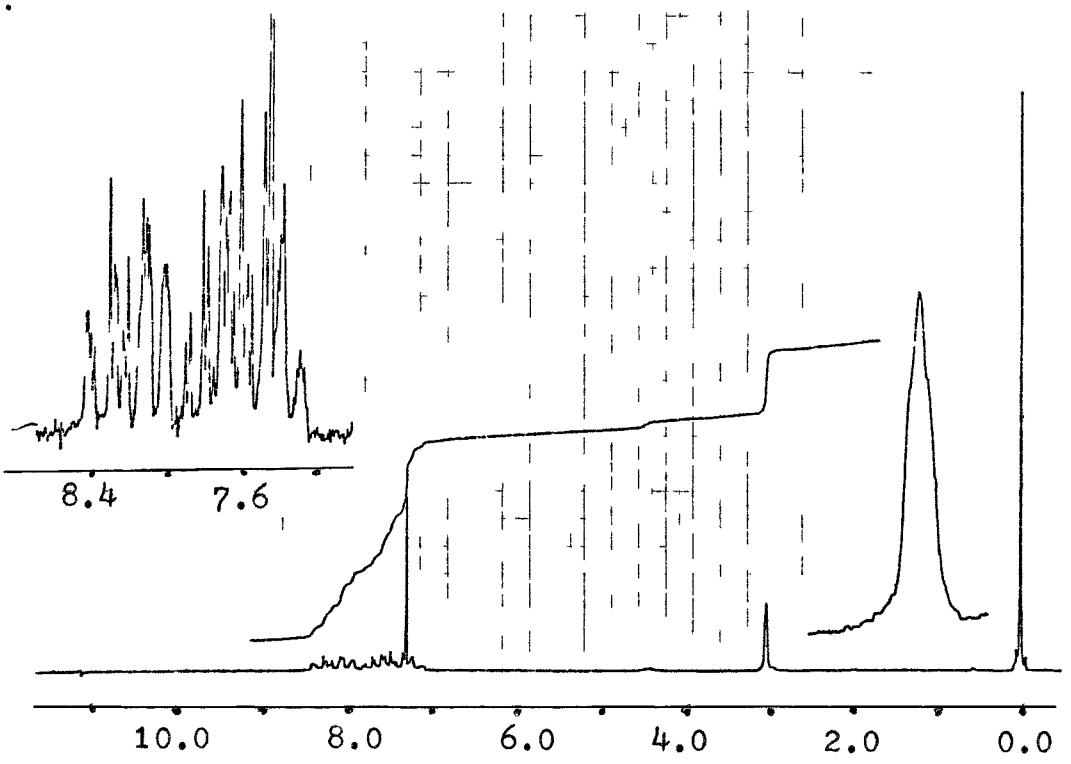


Fig. 50. Double resonance spectrum (aromatic region) of 1-methyl-9-chloroacridine, irradiation at the methyl protons (ν_2 = 181.7 Hz).

Fig. 50.

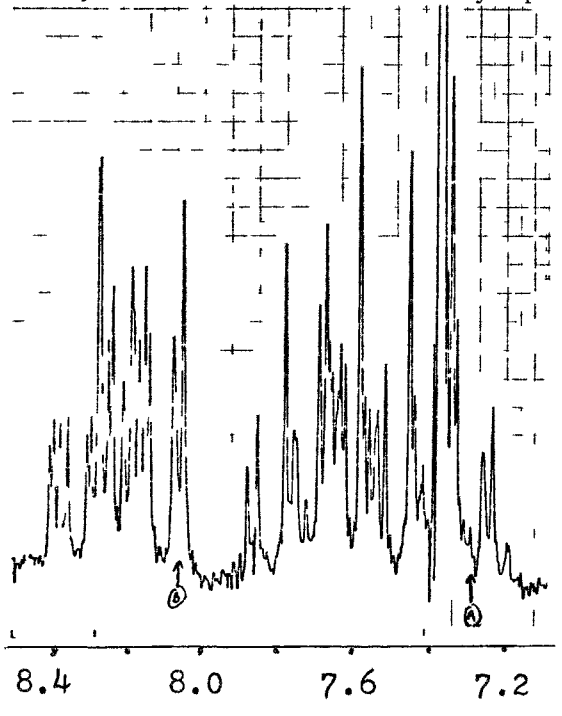


Fig. 51.

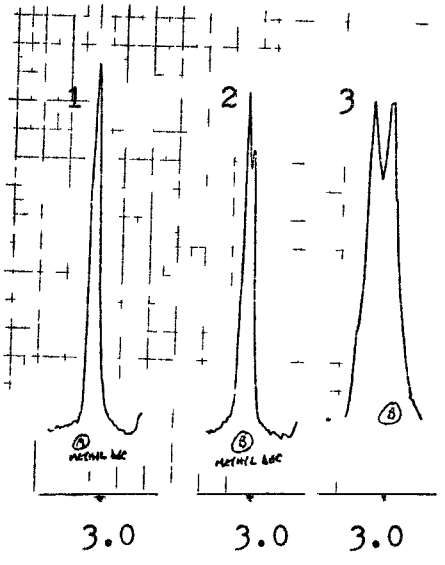


Fig. 51. Double resonance spectra (methyl region) of 1-methyl-9-chloroacridine, 1. irradiation at A (cf. Fig. 50), 2. irradiation at B and 3. plot expansion of 2. to show $\overline{J}$ = 1.01 Hz.

Fig. 52. 60 MHz proton spectrum of 2-methyl-9-chloroacridine in $CDCl_3$. Methyl coupling J = 0.91 Hz.

Fig. 52.

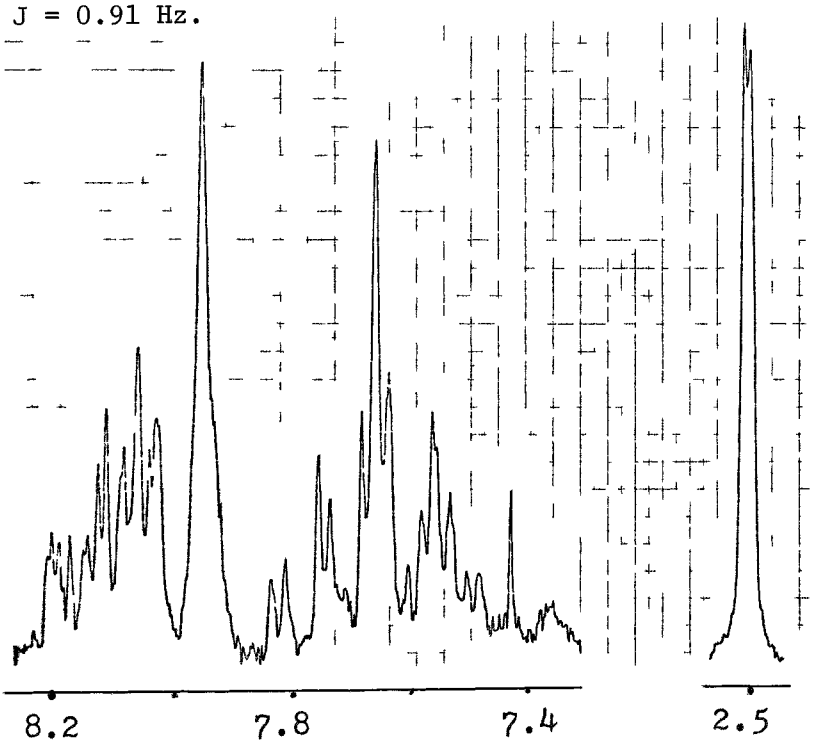


Fig. 53. Double resonance spectrum (aromatic region) of 2-methyl-9-chloroacridine, irradiation of the methyl protons (ν_2 = 150.5).

Fig. 53.

Fig. 54.

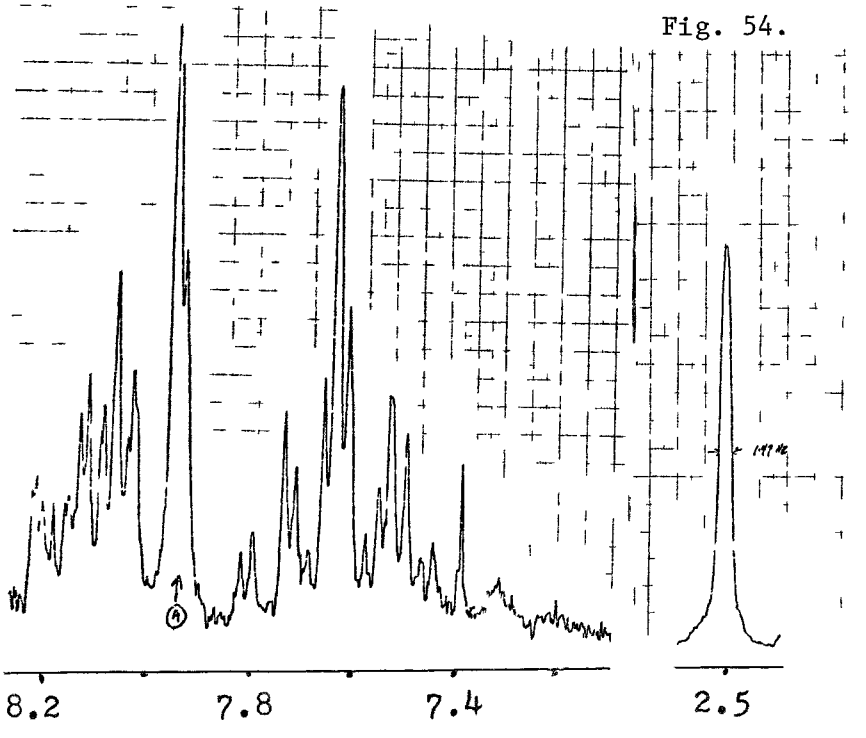


Fig. 54. Double resonance spectrum (methyl region) of 2-methyl-9-chloroacridine, irradiated at A (cf. Fig. 53).

Fig. 55.

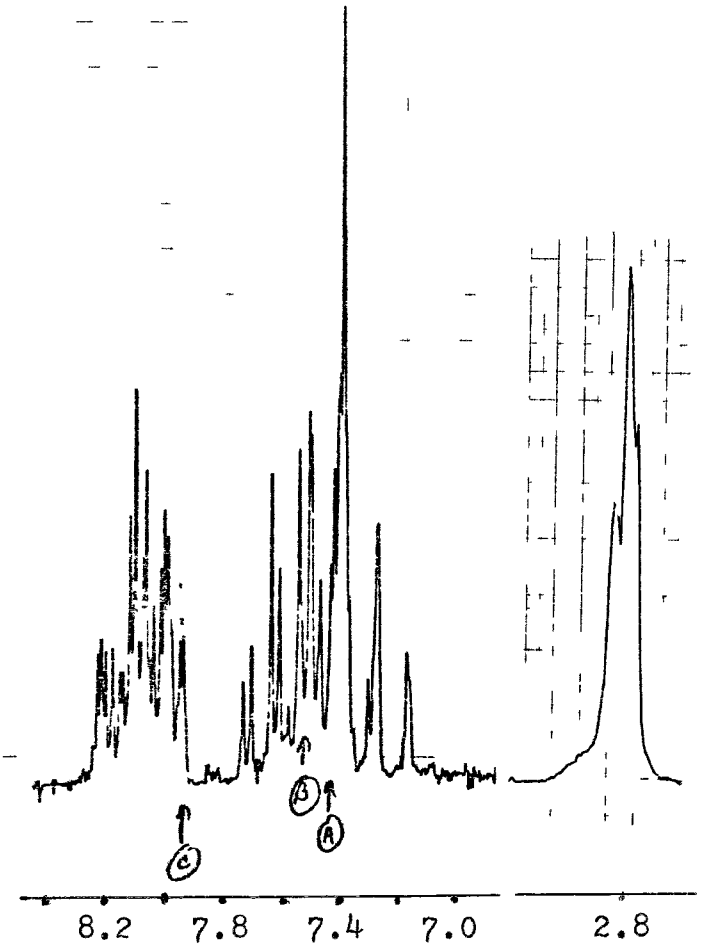


Fig. 55. 60 MHz proton spectrum of 4-methyl-9-chloroacridine in $CDCl_3$.

Fig. 56.

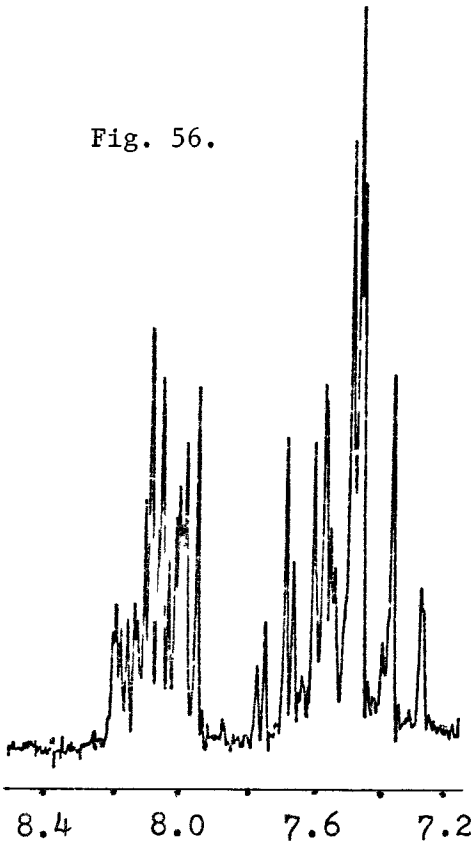


Fig. 57.

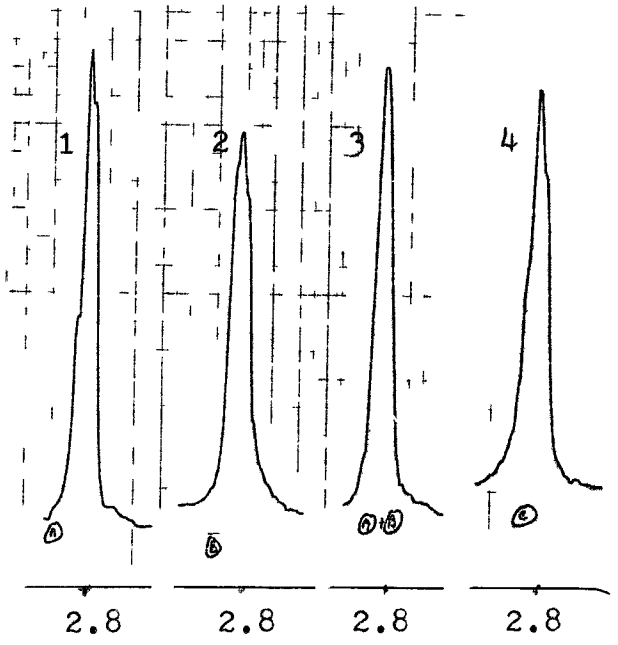


Fig. 56. Double resonance spectrum (aromatic region) of 4-methyl-9-chloroacridine, irradiation of the methyl protons (ν_2 = 170.4 Hz).

Fig. 57. Double resonance spectra (methyl region) of 4-methyl-9-chloroacridine, 1. irradiation at A (cf. Fig. 55), 2. irradiation at B, 3. irradiation at A and B, and 4. irradiation at C.

Table 9.
Proton chemical shifts of methylxanthones in $CDCl_3$ (δ ppm)

Proton	1-methyl	2-methyl	3-methyl	4-methyl
H-1,8	8,28	8.23	8.28	8.26
methyl	2.92	2.43	2.49	2.55

Table 10.
Proton chemical shifts of methylthioxanthones in $CDCl_3$ (δ ppm)

Proton	1-methyl	2-methyl	3-methyl	4-methyl
H-1,8	8.50	8.37	8.56	8.51
methyl	2.91	2.48	2.46	2.36

Table 11.
Proton chemical shifts of methylthioxanthone 10,10-dioxides in $CDCl_3$ (δ ppm)

Proton	1-methyl	2-methyl	3-methyl	4-methyl
methyl	2.74	2.53	2.55	2.90

Table 12.
Proton chemical shifts of methylacridones in DMSO-d_6 (δ ppm)

Proton	1-methyl	2-methyl	3-methyl	4-methyl
NH	11.54	11.69	11.78	10.59
H-1,8	8.19	8.20	8.19	8.18
methyl	2.89	2.43	2.46	2.60

Table 13.
Proton chemical shifts of methyl-9-chloroacridines in $CDCl_3$ (δ ppm)

Proton	1-methyl	2-methyl	3-methyl	4-methyl
methyl	3.03	2.51	--	2.84

The methyl signal of 1-methyl isomers of xanthone, thioxanthone and thioxanthone 10,10-dioxide could not be resolved by any decoupling experiments but appeared as a multiplet with couplings ca. 0.2 Hz. Irradiation of the CH_3 produced decoupling in the high field portion of the aromatic regions. Irradiation of this proton collapsed the 1-methylthioxanthone CH_3 resonance to a singlet with 0.7 Hz linewidth.

These observations led us to expect similar behaviour in the acridone and 9-chloroacridine analogues. Irradiation of the 1-methylacridone methyl gave decoupling in the high field portion of the aromatic region of the spectrum, but decoupling of this proton gave no large methyl splitting. Irradiation of the methyl group of 1-methyl-9-chloroacridine gave decoupling in the low field and high field portions of the aromatic region of the spectrum. Subsequent irradiation of the low field proton surprisingly produced a doublet (J = 1.01 Hz) in the methyl region.

2-Methylthioxanthone, 2-methylacridone and 2-methyl-9-chloroacridine show a doublet for the methyl group with couplings of 0.73, 0.73 and 0.91 Hz respectively. Irradiation of the CH_3 produced some decoupling in the low field portion of the aromatic region, which we ascribe to the proton adjacent to the carbonyl, H-1, in VI and VII. Irradiation of this proton collapses the methyl resonance to a singlet. Supportive evidence for the assignment of H-1 is the absence of the low field multiplet in the spectra of 1-methylxanthone and 1-methylacridone.

These observations led us to expect similar behaviour in 2-methylxanthone and 2-methylthioxanthone 10,10-dioxide. However, the methyl group in these compounds appeared as a rather broad peak with shoulders. Irradiation of the methyl group gave decoupling in the high field

portion of the aromatic region of the spectra, and decoupling of this proton produced a doublet (J = 0.55 Hz) in the methyl region. Incidentally, higher order splitting apparently complicates the methyl absorption of the sulfone compound. Irradiation of the low field proton, H-1, in 2-methylxanthone collapses the methyl doublet to a singlet.

Coupling of both ortho protons in 3-methylxanthone complicated the methyl absorption. Decoupling proton H-1 gave an unresolved peak, but when Brindle, Jones and Miller performed a double irradiation of H-1 and H-2, a doublet (J = 0.55 Hz) was observed in the methyl regions.[5] The methyl signal of 3-methylthioxanthone 10,10-dioxide appeared as a symmetric multiplet with couplings ca. 0.37 Hz. Irradiation of the high field proton produced a doublet (J = 0.55 Hz) in the methyl region.

The 3-methylthioxanthone and 3-methylacridone methyl could not be resolved but appeared as a rather broad peak with shoulders. Irradiation of the methyl group gave decoupling in the low field, mid field and high field portions of the aromatic region of the spectrum, but decoupling in the aromatic region gave no large methyl coupling.

4-Methylxanthone shows a singlet for the methyl group with 1.6 Hz line width at a resolution in which the linewidth of the TMS resonance was 0.4 Hz. Irradiation of the CH_3 produced decoupling in the low field portion of the aromatic region, which we ascribe to the proton adjacent to the carbonyl, H-1. Subsequent decoupling of the proton produced a doublet (J = 0.55 Hz) in the methyl region.

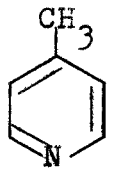
The 4-methyl isomers of thioxanthone, thioxanthone 10,10-dioxide and acridone gave methyl resonances which could not be resolved but appeared as rather broad peaks. Irradiation of the high field proton of

4-methylthioxanthone collapsed the CH_3 signal to a singlet with 0.75 Hz linewidth. Irradiation in the low field portion of the aromatic region of the sulfone analogue collapsed the CH_3 resonance to a singlet with 0.5 Hz linewidth; decoupling the high field portion gave a multiplet with couplings ca. 0.2 Hz in the methyl region. The 4-methyl-9-chloroacridine methyl also could not be resolved and appeared as a multiplet with couplings ca. 0.2 Hz.

Our study of the proton magnetic resonance spectra of the methyl substituted heterocycles described above has revealed for some, coupling of all three different aromatic protons to the methyl, two of the couplings typically being smaller than the third. With the large coupling being on the order of 0.5-1.0 Hz, it was necessary to decouple the aromatic part of the spectrum.

The analysis of the PMR spectrum of toluene indicates the methyl protons are strongly coupled to all five of the aromatic ring protons. The absolute values of the ortho-, meta- and para-methyl, ring coupling constants are 0.75, 0.36 and 0.62 Hz respectively.[24] The presence of two ortho protons in the 2- and 3-methyl heterocycles studied would be expected to complicate the methyl absorption. For this reason, we expected it would be necessary to decouple perhaps two distinctly different regions of the aromatic part of the spectrum in order to see the strong methyl-ring coupling.

Rottendorf and Sternhell have shown that the principal side-chain coupling in a large number of p-disubstituted benzene derivatives is to the ortho rather than to the meta position.[25] The methyl group of γ-picoline (XIII) appeared as a barely resolvable triplet ($J \simeq 0.6$ Hz).



(XIII)

2-Methylthioxanthone, 2-methylacridone and 2-methyl-9-chloroacridine show a doublet for the methyl group with couplings of 0.73, 0.73 and 0.91 Hz respectively, despite the presence of two ortho protons. 2-Methylxanthone and 2-methylthioxanthone 10,10-dioxide also showed a methyl doublet (each J = 0.55 Hz) after decoupling a high field portion of their aromatic regions. Irradiation of the methyl produced some decoupling in the low field portion of the aromatic region, which we ascribe to the H-1 proton. Irradiation of this proton collapses the doublet.

Coupling to both ortho protons complicated the methyl absorption of the 3-methylheterocycles. The methyl coupling to H-4 could however be observed for 3-methylxanthone and 3-methylthioxanthone 10,10-dioxide (J = 0.55 Hz) only after H-2 had been decoupled.

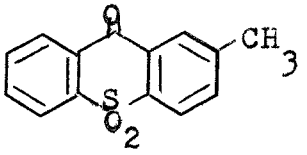
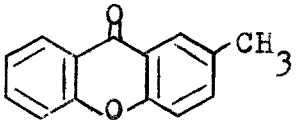
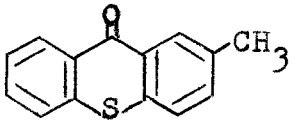
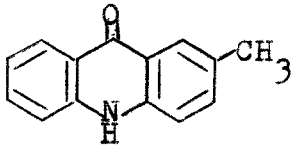
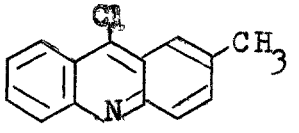
Normally, even after decoupling experiments, the methyl group of the 1-methylheterocycles did not show a strong ortho-benzylic coupling but appeared as a broad singlet or complicated multiplet. In the case of 1-methyl-9-chloroacridine, however, decoupling of a low field proton produced a doublet (J = 1.01 Hz) in the methyl region of the spectrum. Presumably the proton complicating the methyl absorption is H-4 which might resonate at low field since it is ortho to the N-lone pair of electrons.

Supportive evidence for the assignment of H-1 as the proton doing the strong coupling in the 2-methylheterocycles is the absence of the low field multiplet in the spectra of 1-methylxanthone and 1-methylacridone.

All 4-methyl compounds showed broad methyl absorptions or complex multiplets indicating higher order coupling despite the presence of only one ortho proton, H-3. In 4-methylxanthone, decoupling of the low field proton, H-1, resolved the methyl resonance into a doublet (J = 0.55 Hz).

There appears to be a direct dependence of the magnitude of the ortho-benzylic coupling constant between H-1 and the 2-methyl on the electronic nature of the group at the C-9 position. An increase in the electron-withdrawing capacity of this group (C=O > C-Cl) means a decrease in the magnitude of $^{4}J_{H\text{-}1,2\text{-}CH_3}$. Secondly, an enhanced electron-withdrawing capacity of the bridge at position 10 in these tricyclic heteroatomics ($-SO_2-$ > -O- > -NH- > =N-) is connected with a decrease in the magnitude of the ortho-benzylic coupling constant (cf. Table 14).

Table 14.
Experimental ortho-Benzylic Coupling Constants for 2-Methylheterocycles

Molecule	$^{4}J_{H\text{-}1,2\text{-}CH_3}$ (Hz)
	0.55
	0.55
	0.73
	0.73
	0.91

Presumably the geometry of the pathway $^4J_{CC}$, responsible for the ortho-H,CH_3 spin coupling is the same in all 2-methylheterocycles in

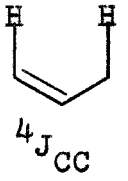
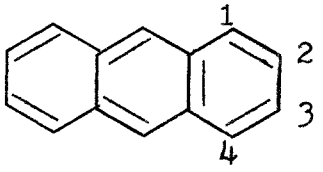


Table 14. However, the σ- and π- contributions which determine in part the values of the coupling constants are different.

A PMR study by Jonathan and co-workers on condensed ring hydrocarbons gives evidence that an increase in the spin coupling constants between adjacent protons was accompanied by a corresponding increase in the calculated bond order of the intervening carbon-carbon bond.[26] Any variation in bond order is accompanied by a change in the distance between coupled protons so that the change in coupling constants is due to changes in the degree of π-bond delocalization produced by orbital overlap. In their study, anthracene (XIV) exhibits an increased π-bond order (0.738)



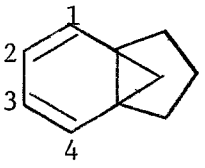
(XIV)

between the C-1 and C-2 carbons which is associated with the larger vicinal coupling constant of 8.3 Hz. A diminished π-bond order (0.586) between the C-2 and C-3 carbons is connected with a smaller vicinal coupling constant of 6.5 Hz.[26]

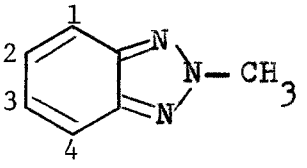
Günther has demonstrated that changes in the degree of π-bond delocalization in cyclic polyenes affects vicinal as well as long range

coupling constants.[27] He explains the trends in going from XV to benzene in terms of σ- and π-contribution changes related to the increase in delocalization of π-electrons in this series (cf. Table 15).

Table 15.
Experimental Cyclic Polyene Coupling Constants (Hz)[27]



(XV)



(XVI)

	(XV)	(XVI)	
^3J_C	9.25	8.65	7.56
^3J_S	5.94	6.79	7.56
^4J	0.58	1.04	1.38
^5J	1.31	1.03	0.68

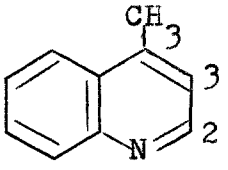
^3J_C is between H-1,2 and ^3J_S between H-2,3.

The gradual increase in the ortho-benzylic coupling constants (cf. Table 14) in going from 2-methylthioxanthone 10,10-dioxide to 2-methyl-9-chloroacridine may be related to the degree of π-bond delocalization in the molecules and more specifically the π-bond order between the intervening C-1 and C-2 bond.

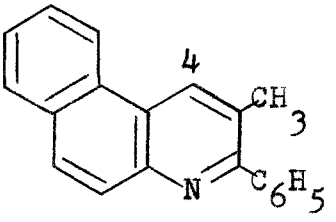
Rottendorf and Sternhell conclude, that in a PMR study on a series of six-membered heterocycles

> ...the magnitude of the ortho side-chain coupling constants appears to be related to the bond order of the aromatic bond separating the methyl group and the aromatic proton in the ortho position.[25]

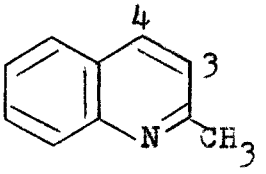
The methyl group of 4-methylquinoline (XVII) gave rise to a doublet (J = 0.95 Hz) due to splitting by the H-3 proton. The methyl group of 3-methyl-2-phenyl-5,6-benzoquinoline (XVIII) also appeared as a doublet (J = 0.83 Hz) due to coupling to the H-4 proton. 2-Methylquinoline (XIX) did not, however, show any large methyl splitting but appeared as a singlet with 0.76 Hz linewidth. In the same spectrum, TMS gave a singlet resonance absorption with 0.35 Hz line width indicating that the ortho coupling in XIX is less than 0.4 Hz.[25]



(XVII)



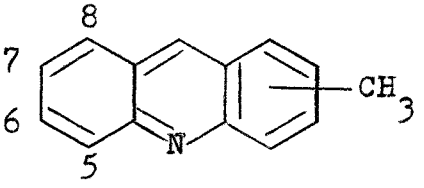
(XVIII)



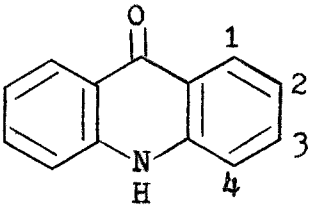
(XIX)

Sciacovelli and von Philipsborn give evidence that indicates methylacridines (XX) exhibit a certain extent of π-bond fixation. In the methyl compounds substituted in ring C the vicinal coupling constants ^3J_C are considerably larger (J_{56} = 8.82 to 8.90 Hz; J_{78} = 8.43 to 8.52 Hz) than ^3J_S (J_{67}= 6.58 to 6.68 Hz).[3] In addition the vicinal coupling constant is larger for the 5,6-bond than for the 7,8 bond implying corresponding bond orders must be different.

In acridone (XXI), the vicinal coupling constants ^3J_C are larger



(XX)



(XXI)

(J_{34} = 8.6; J_{12} = 8.3 Hz) than ^3J_S (J_{23} = 7.0 Hz),[28] indicating an incomplete π-bond delocalization not unlike that in acridine.

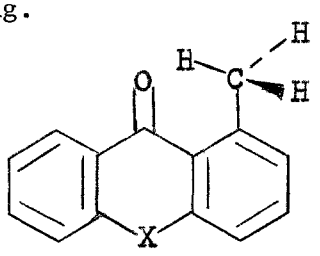
The fact that 2-methylthioxanthone, 2-methylacridone and 2-methyl-9-chloroacridine show methyl doublets in their normal spectra with large ortho-benzylic coupling constants may mean that the degree of π-bond fixation between the C-1 and C-2 carbons in these systems is similar to that in acridine.

Sciacovelli and von Philipsborn have obtained some absolute values for the ortho-, meta- and para-H,CH_3 coupling constants of methylacridines (XX): ortho-(1,2) and ortho-(3,4) ≃ 1.0 Hz, ortho-(2,3) ≃ 0.4 Hz, meta-(1,3) and meta-(2,4) ≃ 0.3 to 0.4 Hz and para-(1,4) ≃ 0.7 Hz.[3]

> Thus the difference between the H,CH_3-coupling across the 1,2- or 3,4- and the 2,3-bond corresponds to the differences observed in the vicinal H,H-coupling and illustrate the π-bond order alternation in this system.[3]

If there is a partially localized π-bond between the C-1 and C-2 carbons in the acridine system, then the methyl resonance of the 1-methyl analogue should be readily resolved into a doublet with a similar coupling constant [ortho-(2,1) ≃ 1.0 Hz]. Sciacovelli and von Philipsborn however give no such coupling constant. 1-Methyl-9-chloroacridine required decoupling of the para proton, H-4, to resolve the ortho coupling, and 1-methylacridone showed no strong ortho methyl coupling after extensive irradiation in the aromatic region. None of the 1-methyl isomers of xanthone, thioxanthone or thioxanthone 10,10-dioxide showed strong ortho couplings but appeared as complex multiplets with coupling constants ca. 0.2 Hz.

In ketonic heterocycles (XXII) it appears the carbonyl group is preventing an effective spin-spin overlap of the methyl protons with the H-2 proton from occurring.



(XXII: X = O, S, SO_2, NH)

The 3-methyl group should similarly couple strongly to the ortho proton, H-4. In none of the heterocycles did the normal methyl resonance appear to show strong coupling to the H-4 proton. However, decoupling in 3-methylthioxanthone 10,10-dioxide resolved the methyl resonance into a doublet. Irradiation in the aromatic region of 3-methylxanthone gave an ortho coupling to the H-4 proton having the same magnitude as the ortho coupling of the 2-methylxanthone methyl to the H-1 proton.

In no case did the 4-methylheterocycles show strong ortho-benzylic coupling to the adjacent H-3 proton. Only in the double resonance spectrum of 4-methylxanthone could an ortho benzylic coupling constant be extracted.

Table 16.
Experimental Methylxanthone ortho-(H,CH_3) Coupling Constants (Hz)

1-Methylxanthone	--
2-Methylxanthone	(1,2) 0.55
3-Methylxanthone	(4,3) 0.55
4-Methylxanthone	(3,4) 0.55

Table 17.
Experimental Methylthioxanthone ortho-(H,CH_3) Coupling Constants (Hz)

1-Methylthioxanthone	--
2-Methylthioxanthone	(1,2) 0.73[a]
3-Methylthioxanthone	--
4-Methylthioxanthone	--

[a] Reference 5 gives 0.77 Hz

Table 18
Experimental Methylthioxanthone 10,10-dioxide ortho-(H,CH_3) Coupling Constants (Hz)

1-Methylthioxanthone 10,10-dioxide	--
2-Methylthioxanthone 10,10-dioxide	(1,2) 0.55
3-Methylthioxanthone 10,10-dioxide	(4,3) 0.55
4-Methylthioxanthone 10,10-dioxide	--

Table 19.
Experimental Methylacridone ortho-(H,CH_3) Coupling Constants (Hz)

1-Methylacridone	--
2-Methylacridone	(1,2) 0.73[a]
3-Methylacridone	--
4-Methylacridone	--

[a] Reference 5 gives 0.82 Hz.

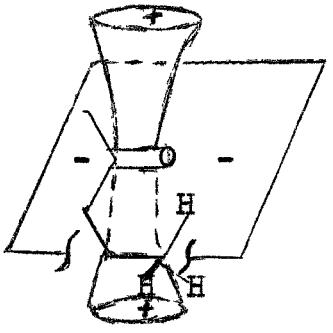
Table 20
Experimental Methyl-9-chloroacridine ortho-(H,CH_3) Coupling Constants (Hz)

1-Methyl-9-chloroacridine	(2,1) 1.01
2-Methyl-9-chloroacridine	(1,2) 0.91
3-Methyl-9-chloroacridine	--
4-Methyl-9-chloroacridine	--

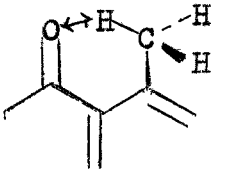
Protons H-1 and H-8 are especially deshielded in the spectra of methyl substituted xanthones, thioxanthones and acridones by the presence of a peri cyclic carbonyl function. The degree of deshielding varies with the nature of the central ring:

$$O, NH < S$$

Low-field shifts are also observed for the 1-methyl protons; the degree of deshielding being about the same for the xanthone, thioxanthone and acridone heterocycles. However, in the case of thioxanthone 10,10-dioxide, the methyl resonance is shifted further upfield. Any variation in the degree of magnetic anisotropic deshielding by the carbonyl group (XXIII) is influenced by the spatial proximity (and steric repulsion) of the methyl protons (XXIV).



(XXIII: deshielding (-) and shielding (+) zones)



(XXIV)

The deshielding of the 4-methyl group also varies with the nature of the central ring:

$$S < O, NH < SO_2$$

Normally the methyl protons were less shielded than the 2- or 3-methyl analogues, except in the case of 4-methylthioxanthone, in which the methyl appeared at a higher chemical shift than the 2- or 3-methyl analogues.

Methyl substitution causes high field shifts for the protons in the same ring. These upfield shifts are brough about by

> ...increased π-electron densities at the corresponding carbon atoms caused by the hyperconjugative interaction of the methyl group with the π-electrons of the aromatic ring, ...

analogous to that described for in the spectral analysis of toluene.[24]

Table 21.
Average Proton Chemical Shifts (δ ppm)[a] of H-1,8 in the Ketonic Heterocycles

Molecule	Unsubstituted	Methyl Substituted
Xanthone	8.32[b]	8.26
Acridone	8.35[c]	8.18
Thioxanthone	8.60[b]	8.49

[a] Measured at the centre of the low field multiplets.

[b] Obtained from reference 29.

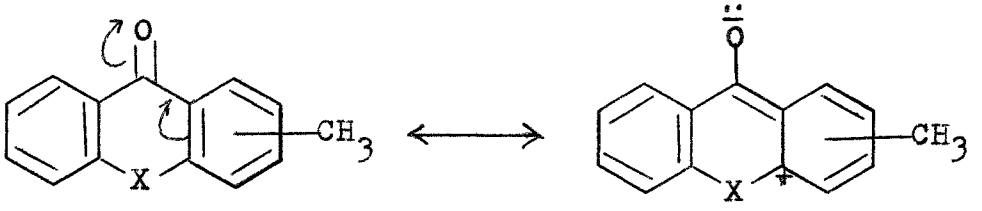
[c] From reference 28.

2.4 Correlation with I.R. Spectroscopic Data

Infrared data suggest variations in the double bond character of the carbonyl group in various isomers of XXV. Any contributions due to

Table 22.
Infrared Carbonyl Stretching Frequencies of Ketonic Methyl heterocycles

Molecule Nucleus	ν_{CO} (cm^{-1})
Acridone	1625-1640
Thioxanthone	1630-1640
Xanthone	1650
Thioxanthone 10,10-dioxide	1675

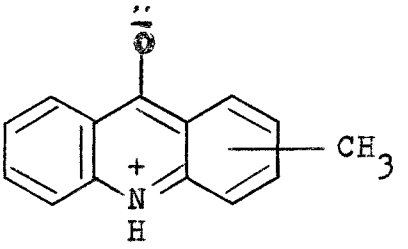


(i) (ii)

(XXV: X = O, S, SO_2 and NH)

canonical forms of type XXV-ii bring about a slight decrease in the double bond character of the carbonyl group.

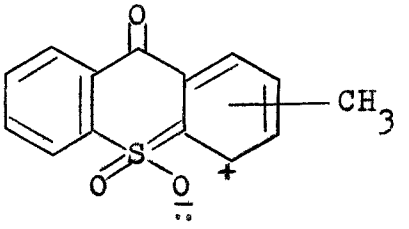
In acridone, the heteroatom assists in decreasing the carbonyl bond order by donating its N-lone pair of electrons into an aromatic ring. The enhanced ring electron density can in turn resonate out onto the carbonyl group leaving a canonical structure represented by XVI.



(XVI)

Consequently there is a decrease in the bond order of the carbonyl group in acridone and a correspondingly low carbonyl frequency of vibration.

In thioxanthone 10,10-dioxide, the sulfone bridge is in competition with the carbonyl group for mobile π-electron density (cf. XXVII).



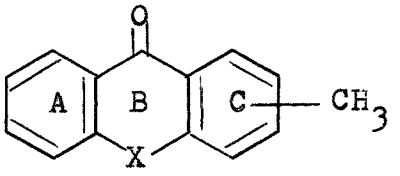
(XXVII)

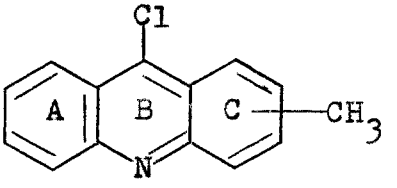
Hence the carbonyl group has an enhanced double bond character, and absorbs at a higher vibrational frequency in the infrared.

In xanthone, the capacity for resonance donation of the heteroatom into an aromatic ring is somewhat less than in the sulfur or nitrogen analogues due to the oxygen's high electron afinity. Consequently, the π-electron density about the aromatic rings is not substantially enhanced, making it less facile for the carbonyl group to withdraw π-electron density from the ring. Hence canonical form XXV-i (X = O) is expected to make a major contribution to the overall resonance hybrid.

2.5 Direction of Continuing Research

In this study of the methyl heteroatomics XXVIII and XXIX, coupling

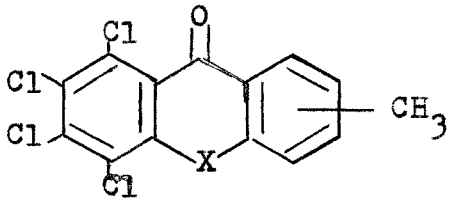


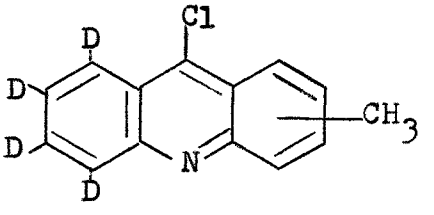


(XXVIII: X = O, S, SO_2, NH) (XXIX)

of all three different aromatic protons to the methyl protons complicated the methyl absorptions. Irradiation of the methyl group produced decoupling in the aromatic region but due to the complexity of the aromatic absorption at 60 MHz, it was not possible to observe individual proton resonances in the aromatic region.

However, without significantly altering the electronic structure of the system (and hence the benzylic side-chain couplings), one can dramatically simplify the PMR spectra by substituting the protons on ring A by chlorine or deuterium atoms (cf. XXX and XXXI respectively),





(XXX) (XXXI)

In doing so, the aromatic region should be simplified significantly to allow for the observation of individual couplings between the three aromatic protons and the methyl groups by using normal double irradiation techniques.

Furthermore, by analysis on an NMR instrument operating at a higher RF frequency (e.g., 100 or 220 MHz spectrometer), one should theoretically be capable of resolving the six-spin $AGKX_3$ system in XXX or XXXI.

EXPERIMENTAL

3.1 Instrumentation and Techniques

1. Melting Points

Melting points were measured on a Kofler hot-stage melting point apparatus. Melting points of the methylacridones were obtained on a Gallenkamp melting point apparatus. These samples were inserted in a sealed capillary at 300°. All m.p.'s are uncorrected.

2. Infrared Spectra

I.R. spectra are of KBr discs measured on a Perkin-Elmer 237B double beam grating infrared spectrophotometer. Abbreviations used when reporting vibrational frequencies are br. = broad, br. m. = broad multiplet, m. = medium intensity, s. = strong intensity and v.s. = very strong intensity.

3. Mass Spectra

Mass spectra were measured with an AEI MS30 double beam, double focussing spectrometer with source temperature ca. 190°, accelerating voltage 4 kV and ionizing electron energy 70 eV. Samples were introduced on a direct insertion probe. Only the most intense peaks were reported.

4. ^{1}H NMR

^{1}H NMR spectra were recorded at 60 MHz on a Bruker WP-60 FT spectrometer for solutions in $CDCl_3$ or DMSO-d_6 with TMS as internal standard. In all cases, oxygen had been removed from the sample. Approximately 0.1 ml of TMS was added to about 1 ml of the nearly saturated solutions of the various samples. The sample was placed in a 5 mm outer diameter PMR tube which was then put onto a vacuum line. After freezing (liquid nitrogen) the sample, any volatile materials were consequently pumped off. This tube was allowed to reach room temperature, at which time the cycle was

repeated. Finally the tube was sealed and the degassed solution was ready for spectral studies.

5. Thin-Layer Chromatography

This was carried out on Silica Gel IB2-F and Aluminum Oxide IB-F Baker-flex sheets supplied by J. T. Baker Chemical Co., and also on Silica Gel 13181 Eastman Chromagram sheets supplied by Eastman Kodak Co.

Visualization of the spots on the developed sheets was accomplished by direct visualization of colored compounds and also by visualization under ultraviolet light (254 nm) for compounds which quench or enhance fluorescence.

6. Microanalysis

All analyses were performed by Dr. F. Pascher Mikroanalytisches Laboratorium, Buschstr., 54, 5300 Bonn, West Germany.

7. Ullmann Reaction Catalyst

The copper bronze powder present during the Ullmann reactions was an analyzed brass alloy. This was supplied by Thorn Smith, Chemists, Inc., Troy, Michigan, U. S. A. Analysis given was 93.30% Cu, 4.98% Sn, 1.55% Zn and 0.08% Pb. The cuprous iodide used was a BDH laboratory reagent.

3.2 2-Carboxy-2'-methyldiphenyl Sulfide

o-Chlorobenzoic acid (2.5 g, 0.016 mole), o-thiocresol (4.0 g, 0.032 mole), dry potassium carbonate (6.6 g, 0.048 mole), cuprous iodide (0.1 g), and copper bronze (0.1 g) were stirred into dry nitrobenzene (20 ml). The reaction mixture was then heated under nitrogen atmosphere to reflux and maintained, with stirring, for 10 minutes.

The dark mixture was cooled, the nitrobenzene distilled off in steam, and the tars filtered off using charcoal. This solution was strongly acidified with hydrochloric acid to pH 1, and the crude product (2.95 g, 75%) was obtained as a tan powder, m.p. 155-170°. Crystallization from dilute ethanol gave 2-carboxy-2'-methyldiphenyl sulfide as a gray powder, m.p. 175-176°, ν_{max} 3350-2250 br (OH), and 1675 cm^{-1} (CO); ^1H NMR (DMSO-d_6) δ 2.29 (3H, S, $ArCH_3$), 6.48-8.06 (8H, complex, ArH) (Found: C, 68.88; H, 4.81; S, 12.92. $C_{14}H_{12}SO_2$ requires C, 68.83; H, 4.95; S, 13.12%), m/e 244 (100%), 197 (33), 193 (67), 184 (17), 137 (33), 91 (81), 77 (16) and 65 (23).

3.3 2-Carboxy-3'-methyldiphenyl Sulfide

This compound was prepared in the same fashion as the 2'-methyl derivative except that m-thiocresol (4.0 g, 0.032 mole) was used instead of the ortho isomer. The precipitate was collected and dried to give the crude product (3.1 g, 80%) as a tan powder melting at 170-174°. Crystallization from methanol gave 2-carboxy-3'-methyldiphenyl sulfide as white needles, m.p. 180-182°, ν_{max} 3350-2250 br (OH), and 1675 cm^{-1} vs (CO); ^1H NMR (DMSO-d_6) δ 2.35 (3H, S, $ArCH_3$) 6.69-8.03 (8H, complex, ArH) (Found: C, 68.70; H, 4.92; S, 12.87. $C_{14}H_{12}SO_2$ requires C, 68.83;

H, 4.95; S, 13.12%) m/e 244 (100%), 197 (16), 184 (30), 137 (71) and 136 (29).

3.4 2-Carboxy-4'-methyldiphenyl Sulfide

p-Thiocresol (4.0 g, 0.032 mole) was added to a cooled solution of sodium (0.75 g, 0.032 mole) dissolved in methanol (15 ml). The methanol was then distilled off at ca. 50 mm pressure and nitrobenzene (20 ml) was added to the residual solid. Potassium carbonate (2.2 g, 0.016 mole), o-chlorobenzoic acid (2.5 g, 0.016 mole), copper bronze (0.1 g) and cuprous iodide (0.1 g) were then added to the solution. The reaction mixture was heated under nitrogen atmosphere to reflux and maintained, with stirring, for 10 minutes.

The mixture was then cooled, the nitrobenzene distilled off in steam and the hot solution filtered using charcoal. Remaining tars were removed by extraction with ether, and the aqueous layer acidified with hydrochloric acid. The precipitate was collected and washed with water to give the crude product (3.3 g, 85%) as a cream colored powder, m.p. 195-210°. Crystallization from aqueous methanol gave 2-carboxy-4'-methyldiphenyl sulfide as white prisms, m.p. 214-216° (lit.[10] m.p. 215-216°) ν_{max} 3350-2250 br (OH) and 1675 cm^{-1} vs (CO); ^1H NMR (DMSO-d_6) δ 2.37 (3H, S, $ArCH_3$), 6.64-8.03 (8H, complex, ArH) m/e 244 (100%), 197 (18), 184 (28), 137 (55), 136 (20), 108 (18), 91 (23) and 65 (18).

3.5 1- and 3-Methylthioxanthone

2-Carboxy-3'-methyldiphenyl sulfide (14.6 g) was stirred with sulfuric acid (146 ml) under nitrogen for 1½ hours at 100°. The cooled

solution was then poured onto ice. This mixture was filtered and the crude product was directly taken up in chloroform. Unchanged starting material was removed by digesting with 10% sodium carbonate. The chloroform layer was then washed with water, dried (magnesium sulfate) and evaporated to dryness. The resultant yellow oil which solidified on standing (8.96 g, 66%), m.p. 55-90°, ^{1}H NMR ($CDCl_3$) δ 2.46 (54%, s, Ar-3-CH_3), 2.91 (46%, S, Ar-1-CH_3) and 7.2-8.5 (complex, ArH) proved to be a 46:54 mixture of 1- and 3-methylthioxanthone respectively.

This material was dissolved in a minimum volume of toluene and chromatographed on 60-100 mesh Florisil. Elution with hexane, hexane: ether, 9:1, 8:2 and 7:3 gave two bands which were examined by t.l.c. (Eastman Chromagram Sheet; CCl_4). The first fraction (R_f 0.81) yielded 1-methylthioxanthone (3.75g, 28%) as pale yellow blades (from hexane), m.p. 93-95°, ν_{max} 1635 cm^{-1} s (CO); (Found: C, 74.49; H, 4.44; S, 13.81. $C_{14}H_{10}SO$ requires C, 74.31; H, 4.45; S, 14.17%) m/e 226 (100%), 225 (38), 198 (15), 197 (43), 165 (13) and 152 (10). The second band (R_f 0.58) afforded 3-methylthioxanthone (3.87 g, 29%) as pale yellow needles (from hexane) melting at 115-116°, ν_{max} 1630 cm^{-1} s (CO); (Found: C, 74.17; H, 4.44; S, 13.93. $C_{14}H_{10}SO$ requires C, 74.31, H, 4.45; S, 14.17%) m/e 226 (100%), 198 (19), 197 (40), 165 (9), 152 (7), 99 (7) and 69 (8).

3.6 2-Methylthioxanthone

2-Carboxy-4'-methyldiphenyl sulfide (15 g) was cyclised by sulfuric acid (150 ml) in the same fashion described for the preparation of 1- and 3-methylthioxanthone. The precipitate (11.6 g, m.p. 112-113°) was dissolved in chloroform and extracted with 10% sodium carbonate, washed with

water and dried (magnesium sulfate). 2-Methylthioxanthone crystallized from ethanol in yellow prisms (8.4 g, 60%), m.p. 122-124° (lit.[11] m.p. 123°) ν_{max} 1630 cm^{-1} s (CO); m/e 226 (100%), 225 (10), 198 (12), 197 (36) and 165 (8).

3.7 4-Methylthioxanthone

2-Carboxy-2'-methyldiphenyl sulfide (15 g) was cyclodehydrated by sulfuric acid (150 ml) in the same manner described for the preparation of 1- and 3-methylthioxanthone. The crude product (11.8 g, m.p. 136-140°) was dissolved in chloroform and extracted with 10% sodium carbonate, washed with water and dried. Evaporation and crystallization from ethanol gave 4-methylthioxanthone as yellow needles (9.1 g, 66%), m.p. 146-148°, ν_{max} 1630 cm^{-1} s (CO) (Found: C, 74.33; H, 4.34; S, 14.04. $C_{14}H_{10}SO$ requires C, 74.31; H, 4.45; S, 14.17%) m/e 226 (100%), 198 (12), 197 (35) and 165 (9).

3.8 1-Methylthioxanthone 10,10-dioxide

1-Methylthioxanthone (3.0 g) was dissolved in 50 ml of hot glacial acetic acid. The solution was heated to reflux and hydrogen peroxide (18 ml, 30%) was added in 6 ml portions at half hour intervals. The reaction mixture was maintained at reflux, with stirring, for 3 hours. A pale yellow crystalline solid separated upon cooling, which after filtration and drying weighed 3.0 g (88%) and melted at 201-202°. Pouring this filtrate over ice gave 0.07 g (2%) of a pale yellow powder, m.p. 190-197°. The former material (3.0 g) was then dissolved in chloroform and passed through a column of acid-washed alumina. The product came

through in the first 200 ml portion of chloroform and a yellow band remained at the top of the column. 1-Methylthioxanthone 10,10-dioxide (2.6 g) was obtained as pale yellow rods (from glacial HOAc), m.p. 201-203°, ν_{max} 1675 cm^{-1} s (CO); (Found: C, 65.02; H, 3.93; S, 12.31. $C_{14}H_{10}SO_3$ requires C, 65.10; H, 3.90; S, 12.41%) m/e 258 (100%), 210 (60), 166 (18), 165 (80), 136 (18), 89 (21), 76 (18) and 63 (23).

3.9 2-Methylthioxanthone 10,10-dioxide

2-Methylthioxanthone (3.0 g) was oxidized in the same way as the 1-methyl derivative to yield a yellow solid, which weighed 2.9 g (85%) and melted at 200-202°. Pouring the filtrate over ice gave 0.2 g (6%) of a yellow powder, m.p. 174-180°. Standard workup chromatography of 2.4 g of the former material (elution with chloroform) gave 2-methylthioxanthone 10,10-dioxide (2.0 g) as white needles (from glacial HOAc), m.p. 204-206° (lit.[11] m.p. 199°) ν_{max} 1675 cm^{-1} s (CO). m/e 258 (35%), 211 (15), 210 (100), 181 (18), 165 (48), 150 (18) and 136 (35).

3.10 3-Methylthioxanthone 10,10-dioxide

Oxidation of 3-methylthioxanthone (3.0 g) with 30% hydrogen peroxide in glacial HOAc by the usual method gave light yellow needles, which after filtration and drying weighed 3.0 g (88%) and melted at 202-204°. Pouring the filtrate over ice gave 0.1 g (3%) of a light yellow powder melting at 184-192°. The former product (3.0 g) was chromatographed over acid-washed alumina. Elution with chloroform gave 3-methylthioxanthone 10,10-dioxide (2.5 g) as white needles (from glacial HOAc), m.p. 206-207°, ν_{max} 1675 cm^{-1} vs (CO); (Found C, 64.97; H, 3.89; S, 12.43. $C_{14}H_{10}SO_3$ requires C, 65.10;

H, 3.90; S, 12.41%) m/e 258 (56%), 211 (15), 210 (100), 165 (61), 150 (18) and 136 (22).

3.11 4-Methylthioxanthone 10,10-dioxide

Oxidation of 4-methylthioxanthone (3.0 g) in the manner described for the preparation of 1-methylthioxanthone 10,10-dioxide gave 2.6 g (76%) of yellow leaves melting at 181-182°. After pouring the filtrate over ice, an additional 0.5 g (15%) of a yellow powder, m.p. 169-175°, was obtained. The former product (2.6 g) was chromatographed over acid-washed alumina. Chloroform eluted 4-methylthioxanthone 10,10-dioxide (2.0 g) as white leaves (from glacial HOAc), m.p. 181-182° (lit.[12] m.p. 172°), ν_{max} 1675 cm^{-1} vs (CO) m/e 258 (75%), 211 (18), 210 (100), 181 (27), 166 (20), 165 (83), 136 (58), and 63 (19).

3.12 N-o-Tolylanthranilic Acid

A mixture of o-toluidine (13.0 g, 0.121 mole), o-chlorobenzoic acid (4.0 g, 0.026 mole), potassium carbonate (4.0 g, 0.029 mole), copper powder (1.0 g) and copper bronze (1.0 g) was refluxed, with stirring, for 3½ hours in amyl alcohol (20 ml). The resulting mixture was cooled, then steam distilled and finally filtered (charcoal). Acidification (pH 1) of the filtrate with dilute hydrochloric acid gave the product. Crystallization from aqueous acetone afforded N-o-tolylanthranilic acid (4.0 g, 69%) as a pale yellow crystalline solid, m.p. 191-193° (lit.[15] m.p. 189°), ν_{max} 3300 m (NH), 3250-2350 br (OH) and 1650 cm^{-1} s (CO), ^1H NMR ($CDCl_3$) δ 2.28 (3H, s, $ArCH_3$), 6.56-7.64 (7H, complex, ArH), 8.05 (1H, ddd, $^3J_{3,4}$ = 7.97 Hz $^4J_{3,5}$ = 1.65 Hz, $^5J_{3,6}$ = 0.55 Hz, H-3) and 8.95 br (1H, s, NH); m/e 227

(70%), 210 (15), 209 (100), 208 (23), 180 (68), 90 (15), 77 (15) and 65 (15).

3.13 N-m-Tolylanthranilic Acid

m-Toluidine (26.0 g, 0.243 mole), o-chlorobenzoic acid (8.0 g, 0.052 mole), potassium carbonate (8.0 g, 0.058 mole), copper powder (1.0 g), copper bronze (1.0 g) and amyl alcohol (40 ml) were reacted in the manner described for N-o-tolylanthranilic acid to give N-m-tolylanthranilic acid (9.2 g, 79%) as a buff colored powder, m.p. 136-137° (lit.[16] 137°) (from aqueous acetone) ν_{max} 3315 m (NH), 3250-2350 br (OH) and 1655 cm^{-1} s (CO); ^1H NMR ($CDCl_3$) δ 2.35 (3H, s, $ArCH_3$), 6.58-7.50 (7H, complex, ArH), 8.05 (1H, ddd, $^3J_{3,4}$ = 8.0 Hz, $^4J_{3,5}$ = 1.6 Hz, $^5J_{3,6}$ = 0.55 Hz, H-3) and 9.60 br (1H, s, NH); m/e 277 (53%), 210 (15), 209 (100), 208 (23), 180 (38), 77 (13) and 65 (18).

3.14 N-p-Tolylanthranilic Acid

A mixture of p-toluidine (21.0 g, 0.196 mole), o-chlorobenzoic acid (8.0 g, 0.052 mole), potassium carbonate (8.0 g, 0.058 mole), copper powder (1.0 g) and copper bronze (1.0 g) was heated for 3 hours at 120°. The resulting mixture was steam distilled, then filtered using charcoal. After cooling, the filtrate was acidified with dilute HCl, and the precipitated product was collected and dried. N-p-Tolylanthranilic acid (8.2 g, 69%) crystallized from aqueous acetone as a pale yellow crystalline solid, melting at 200-201° (lit.[14] m.p. 193-194°) ν_{max} 3315 m (NH), 3250-2350 br (OH) and 1650 cm^{-1} s (CO); ^1H NMR ($CDCl_3$) δ 2.35 (3H, s, $ArCH_3$), 6.70-7.34 (7H, complex, ArH), 8.04 (1H, ddd, $^3J_{3,4}$ = 8.0 Hz), $^4J_{3,5}$ = 1.6 Hz,

$^5J_{3,6}$ = 0.55 Hz), and 9.23 br (1H, s, NH) m/e 227 (66%), 210 (14), 209 (100), 208 (28) and 180 (34).

3.15 1- and 3-Methylacridone

A mixture of N-m-tolylanthranilic acid (4.0 g) in phosphorus oxychloride (8 ml) was refluxed for 10 minutes. The cooled solution was diluted with chloroform (50 ml) and added with stirring to aqueous ammonia (1 ℓ, 5%). The chloroform layer was separated and the aqueous alkaline solution further extracted with chloroform. The combined chloroform extracts were directly dried ($MgSO_4$) and concentrated to give a mixture of 1- and 3-methyl-9-chloroacridine.

The crude mixture of 9-chloroacridines was heated with aqueous hydrochloric acid (50 ml, 1 M) for 2 hours at 100°. Material which proved to be a 55:45 mixture of 1- and 3-methylacridone was deposited as a yellow solid (3.5 g, 95%), melting above 300°, ^{1}H NMR (DMSO-d_6) δ 2.5 (45%, s, Ar-3-CH_3), 3.0 (55%, s, Ar-1-CH_3), 6.9-8.3 (complex, ArH) and 11.7 br (s, NH).

3.16 1-Methyl-9-chloroacridine

A solution of N-m-tolylanthranilic acid (30 g) in phosphorus oxychloride (60 ml) was reacted in the same manner described for 1- and 3-methylacridone. Work-up gave a greenish brown solid (30 g) which was shown by NMR to be a 55:45 mixture of 1- and 3-methyl-9-chloroacridine, ^{1}H NMR ($CDCl_3$) δ 2.5 (45%, s, Ar-3-CH_3), 3.0 (55%, s, Ar-1-CH_3) and 7.1-8.5 (complex, ArH).

The foregoing mixture (30 g) containing 1- and 3-methyl-9-chloroacridine was crystallized from benzene to give 1-methyl-9-chloroacridine as a greenish-yellow solid (10 g) melting at 94-95° (lit.[17] m.p. 93-95°) ν_{max} 1635 cm^{-1} m (conj. C=N) m/e 229 (36%), 227 (100), 226 (17), 192 (29), 191 (18) and 190 (17).

3.17 3-Methylacridone

The foregoing filtrate (from the synthesis of 1-methyl-9-chloroacridine) evaporated to dryness and refluxed with aqueous hydrochloric acid (100 ml, 1 M) gave after 20 minutes a precipitate (13.28 g) which was shown by t.l.c. to be a mixture of isomers. After 25 minutes, 3-methylacridone was deposited as a yellow solid (1.22 g), m.p. 337-340° (lit.,[17] 332-335°) ν_{max} 3300-2900 br. m.(NH), and 1635 cm^{-1} s (CO); m/e 209 (100%), 208 (13), 180 (22), 152 (7) and 77 (9).

3.18 1-Methylacridone

The initially orange solution became yellow when a mixture of 1-methyl-9-chloroacridine (2.5 g) in aqueous hydrochloric acid (50 ml, 1 M) was refluxed for 2 hours. After cooling to room temperature, the product was filtered off and washed with water to yield 1-methylacridone as a yellow solid (1.8 g, 78%), m.p. 322-325° (lit.,[18] m.p. 318°); ν_{max} 3325-2900 br. m. (NH) and 1635 cm^{-1} s (CO), m/e 209 (100%), 208 (50), 180 (20), 179 (13), 152 (8), 77 (11) and 76 (8).

3.19 2-Methyl-9-chloroacridine

A mixture of N-p-tolylanthranilic acid (2.5 g) in phosphorus oxychloride (5 ml) was reacted in the manner described for 1- and 3-methylacridone. The product was isolated as a yellow solid. Crystallization from ethanol gave 2-methyl-9-chloroacridine (2.2 g, 88%), m.p. 116-118° (lit.,[14] m.p. 117-118°) ν_{max} 1635 cm^{-1} m (conj. C=N) m/e 229 (33%), 227 (100), 226 (15), 192 (21), 191 (15) and 190 (13).

3.20 2-Methylacridone

N-p-Tolylanthranilic acid (10 g) and phosphorus oxychloride (20 ml) were reacted in the usual manner to give 2-methyl-9-chloroacridine. A mixture of the crude 9-chloroacridine in aqueous hydrochloric acid (100 ml, 1 M) was heated for 2 hours at 100°. The material which separated as a yellowish-green deposit was collected, washed with water and dried to give 8.83 g (96%) of 2-methylacridone, melting above 300°. This material was then crystallized from DMSO to afford a yellow powder, m.p. 320-323° (lit.,[19] m.p. 338°) ν_{max} 3290-2950 br. m. (NH) and 1635 cm^{-1} s (CO); m/e 209 (100%), 208 (33), 180 (23), 179 (8), 152 (7) and 77 (9).

3.21 4-Methyl-9-chloroacridine

N-o-Tolylanthranilic acid (5.0 g) and phosphorus oxychloride (10 ml) were reacted in the usual manner to afford a greenish-brown solid. The product was crystallized from acetone by slow addition of water to yield 4-methyl-9-chloroacridine (4.5 g, 90%) m.p. 88-90° (lit.[18] m.p. 96-97°) ν_{max} 1625 cm^{-1} s (conj. C=N), m/e 229 (33%), 227 (100), 226 (12), 193 (14), 192 (18) and 191 (17).

3.22 4-Methylacridone

N-o-Tolylanthranilic acid (5.0 g) and phosphorus oxychloride (10 ml) were reacted in the usual manner to yield 4-methyl-9-chloroacridine.

The crude 9-chloroacridine was then hydrolysed in aqueous hydrochloric acid (50 ml, 1 M) for 1 hour at 100°. The product was isolated as a yellow solid (4.3 g, 93%) melting above 300°. Crystallization from DMSO gave 4-methylacridone, m.p. 333-335° (lit.,[20] m.p. 345-346°) ν_{max} 3350-2830 br. m.(NH), and 1625 cm^{-1} s (CO); m/e 209 (100%), 208 (28), 180 (28), 152 (8) and 77 (7).

APPENDIX

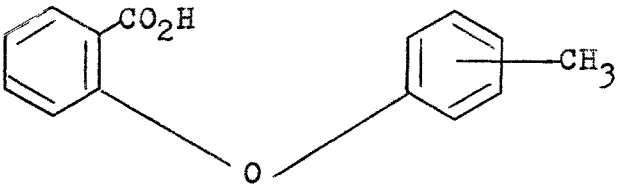
^{13}C NMR

Natural abundance proton decoupled ^{13}C NMR spectra were obtained on a Bruker WP-60 FT spectrometer operating at 15.08 MHz in the pulsed Fourier transform mode. The probe temperature was approximately 32 ± 3°C. Typically, sweep-widths of 3750 Hz with 4096 plot data points were used. Consequently, chemical shift values are accurate to within ± 1.0 Hz. Normally a pulse width of 3.1 μsec and an aquisition time of 1.1 sec were used to obtain each spectrum. In some cases, however, a pulse width of 1.1 μsec was used. The deuterium of the solvent ($CDCl_3$ or DMSO-d_6) was used as the internal lock-signal and all chemical shifts are reported as δ (ppm) downfield from the TMS added as internal reference. When the TMS concentration was too low to show a signal, chemical shifts were measured from the centre peak of the solvent signal and corrected using the appropriate expression:

$$\delta_{TMS} = \delta_{DMSO\text{-}d_6} + 39.5 \qquad \text{OR} \qquad \delta_{TMS} = \delta_{CDCl_3} + 77.0$$

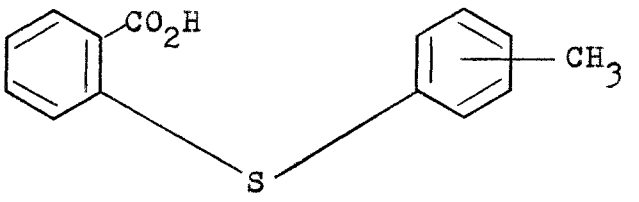
Carbon-13 spectra were obtained of solid samples in nearly saturated solutions in $CDCl_3$ or in DMSO-d_6. Approximately 0.1 ml of TMS was added to about 1 ml of the nearly saturated solutions of the various samples. Samples were placed in 5 or 10 mm NMR tubes (depending on the concentrations) and each sample tube was then mounted in the appropriately sized probe.

Table 23. ^{13}C Shieldings for 2-Carboxy-x'-methyldiphenyl Ethers in $CDCl_3$ (δ ppm)



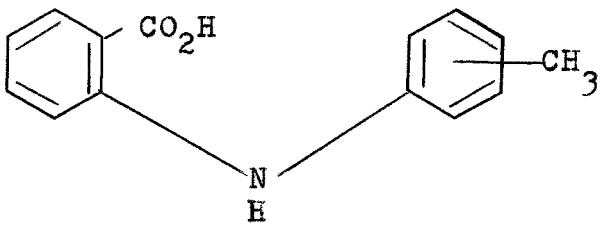
1'-Methyl	167.3	157.7	152.5	134.9	133.7	132.1	130.6	127.8
	125.9	123.0	120.9	116.2	16.1			
2'-Methyl	169.9	157.6	156.2	140.2	134.7	132.9	129.7	125.0
	123.2	120.8	119.9	119.4	116.3	21.2		
3'-Methyl	169.0	157.9	153.4	134.6	134.2	132.9	130.6	123.1
	120.3	119.6	118.5	20.7				

Table 24. ^{13}C Shieldings for 2-Carboxy-x'-methyldiphenyl sulfides in DMSO-d_6 (δ ppm)



1'-Methyl	167.4	142.4	141.2	136.5	132.4	131.2	130.1	127.6
	125.9	124.5	20.1					
2'-Methyl	167.4	141.9	139.6	135.5	132.2	130.9	129.9	127.9
	127.0	124.6	20.8					
3'-Methyl	167.4	154.5	142.4	139.2	136.0	135.4	132.3	130.7
	128.7	127.6	126.7	124.4	20.8			

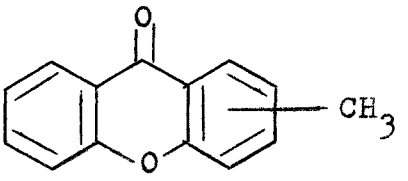
Table 25. ^{13}C Shieldings for N-Tolylanthranilic Acids in $CDCl_3$ (δ ppm)



o-Tolyl	174.1	149.9	138.8	135.4	133.7	132.7	131.3	126.9
	125.4	125.1	116.7	113.9	111.3	109.9[a]	18.1	
m-Tolyl	172.7	149.1	140.4	139.4	135.2	132.7	129.3	125.0
	123.9	120.2	117.1	114.2	21.4			
p-Tolyl	173.7	149.7	137.7	135.3	134.2	132.7	130.1	123.9
	116.8	113.9	111.3	20.9				

[a]Signal possibly not due to expected nucleus.

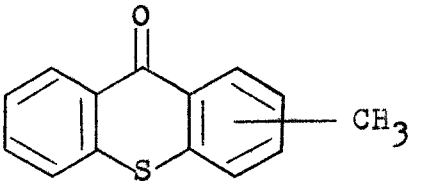
Table 26. ^{13}C Shieldings for Methylxanthones in $CDCl_3$ (δ ppm)



1-Methyl	178.6	157.3	155.1	146.3	143.5	141.8	134.1	133.4
	126.5	123.4	122.6	117.3	115.9	23.1		
2-Methyl	176.8	156.0	154.2	135.8	134.4	133.5	126.5	125.9
	123.6	121.7	121.3	117.8	117.6	20.7		
3-Methyl	176.9	169.2[a]	156.2	146.3	134.5	133.9	127.0	126.7
	126.5	125.4	123.7	122.0[a]	119.7[a]	118.0	117.7	21.9
4-Methyl	148.0	135.7	134.6	132.5	131.2	127.3	126.8	124.5
	123.9	123.5	121.9	118.1	15.8			

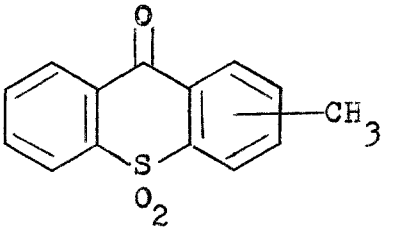
[a]Signal possibly not due to expected nucleus.

Table 27. ^{13}C Shieldings for Methylthioxanthones in $CDCl_3$ (δ ppm)



1-Methyl	182.5	147.0	144.3	143.9	138.5	136.0	131.7	131.2
	130.2	129.7	126.1	125.2	124.3	24.8		
2-Methyl	179.7	137.3	136.2	135.9	133.5	131.9	129.7	129.5
	129.1	128.8	125.9	125.7	21.1			
3-Methyl	179.7	143.3	142.3	137.3	132.0	129.8	127.9	127.0
	126.1	125.9	125.7	21.6				
4-Methyl	177.8	136.9	134.1	133.4	132.3	129.8	129.0	127.7
	126.4	125.6	19.4					

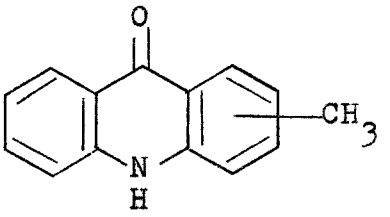
Table 28. ^{13}C Shieldings for Methylthioxanthone 10,10-dioxides in $CDCl_3$ (δ ppm)



1-Methyl	181.7	147.9[a]	142.9	142.1	139.5	137.2	134.0	133.5
	133.4	133.2	130.2[a]	129.0	127.8[a]	123.0	122.0	22.8
2-Methyl	178.7	144.4	141.3	138.4	135.3	134.6	133.2	130.9
	130.6	129.5	129.2	123.7	123.6	21.7		
3-Methyl	178.1	146.6	141.0	134.6	134.1	133.2	129.5	129.2
	128.4	123.8	123.6	22.0				
4-Methyl	178.5	142.4	138.2	137.4	134.9	133.0	132.4	131.0
	129.7	128.7	127.4	123.6	19.9			

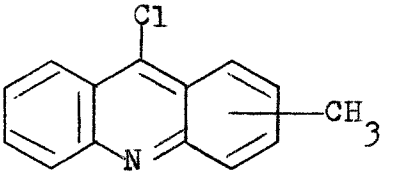
[a]Signal possibly not due to expected nucleus.

Table 29. ^{13}C Shieldings for Methylacridones in DMSO-d_6 (δ ppm)



1-Methyl	179.1	142.5	140.4	140.1	132.9	132.3	126.1	123.4
	121.7	120.6	116.6	115.4	23.5			
2-Methyl	140.8	140.5	139.1	138.0	134.9	133.2	130.4	130.1
	126.0	125.1	120.7	120.4	117.3	20.5		
3-Methyl	176.9	144.1	141.5	141.3	133.5	126.4	123.1	121.2
	120.9	119.0	117.6	116.9	21.9			
4-Methyl	141.1	135.3	134.0	133.2	125.7	125.3	124.0	121.2
	120.7	120.4	118.1	17.7				

Table 30. ^{13}C Shieldings for Methyl-9-chloroacridines in $CDCl_3$ (δ ppm)



1-Methyl	150.7	148.0	141.2	135.4	130.3	130.0	129.6	129.5
	129.3	128.4	126.8	125.0	26.4			
2-Methyl	148.3	147.8	139.9	137.1	133.5	130.6	130.1	129.6
	129.4	126.7	125.6	124.5	122.6	116.6[a]	22.1	
4-Methyl	148.5	148.1	140.8	137.8	135.3	130.4	129.9	129.8
	126.7	124.5	124.2	124.0	122.6	18.6		

[a]Signal possibly not due to expected nucleus.

Bibliography

1. R. A. Spragg, unpublished data (1973).

2. G. A. Olah and P. von R. Schleyer, Carbonium Ions, Vol. 2, Wiley-Interscience, 865 (1970).

3. O. Sciacovelli and W. von Philipsborn, Organic Magnetic Resonance, Vol. 3, 339 (1971).

4. S. M. Vines, M.Sc. thesis, Brock University, St. Catharines, Ontario (1971).

5. I. D. Brindle, T. R. B. Jones and J. M. Miller, unpublished data, Brock University, St. Catharines, Ontario (1976).

6. F. Ullmann and M. Zlokasoff, Ber., 38, 2111 (1905).

7. A. A. Goldberg and A. H. Wragg, J. Chem. Soc., 4227 (1958).

8. Ibid., 4237 (1958).

9. P. P. Doyle, B.Sc. thesis, Brock University, St. Catharines, Ontario (1976).

10. J. Goldberg, Ber., 37, 4526 (1904).

11. F. Mayer, Ber., 43, 584 (1910).

12. F. Ullmann and A. Lehner, Ber., 38, 740 (1905).

13. H. Gilman and J. W. Diehl, J. Org. Chem., 24. 1914 (1959).

14. N. S. Drozdov, J. Gen. Chem. (U.S.S.R.) 6, 1641 (1936).

15. K. Lehmstedt, W. Bruns and H. Klee, Ber., 69B, 2399 (1936).

16. K. Lehmstedt and K. Schrader, Ber., 70B, 838 (1937).

17. A. Ledochowski, B. Stefanska and B. Kozinska, Roczniki Chem., 38(3), 421 (1964).

18. R. M. Acheson and R. G. Bolton, J.C.S. Perkin I, 650 (1975). Obtained m.p.'s through a private communication.

19. C. Graebe and J. Kahn, Annalen, 279, 272 (1894).

20. A. Pictet and A. Hubert, Ber., 29, 1191 (1896).

21. H. Budzikiewicz, C. Djerassi and D. H. Williams, Mass Spectrometry of Organic Compounds, Holden-Day Inc., 558 (1967).

22. S. Meyerson, H. Drews and E. K. Fields, Anal. Chem., 36, 1294 (1964).

23. R. M. Acheson, R. T. Aplin and R. G. Bolton, Organic Mass Spectrometry, 12(8), 518 (1977).

24. M.P. Williamson, R. J. Kostelnik and S. M. Castellano, J. Chem. Phys., 49, 2218 (1968).

25. H. Rottendorf and S. Sternhell, Aust. J. Chem., 17, 1315 (1964).

26. N. Jonathon, S. Gordon and B. P. Dailey, J. Chem. Phys., 36, 2443 (1962).

27. H. Günther, Tetrahedron Letters, 2967 (1967).

28. R. H. Altiparmakian, H. Bohler, B. L. Kaul and F. Kehrer, Helvetica Chemica Acta, 55, 85 (1972).

29. R. H. Martin, N. Defay, F. Geerts-Evrard, P. H. Givin, J. R. Jones and R. W. Wedel, Tetrahedron, 21, 1833 (1965).